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Table of Contents

PATHOLOGICAL CONDITIONS ASSOCIATED WITH DISTURBANCE OF THE THYREOID GLAND WITH SPECIAL REFERENCE TO THE MODERN VIEWS ON IODINE THERAPY.[1]

By O. A. A. DIETHELM, M.B., Ch.M. (Sydney),
Honorary Physician and Lecturer in Clinical Medicine, Saint Vincent's Hospital, Sydney.

INTERRELATIONSHIP OF ALL THE ENDOCRINE GLANDS.

IN every question into which endocrinology enters, it is necessary to bear in mind the important fact of the interdependence of the glands which constitute the system. We are much too apt to regard each as an independent entity instead of considering each as a member of a hierarchy, the whole of which is liable to be deranged when one of the members is seriously affected. This is further borne out by the misleading fashion of speaking of "hyper" or "hypo" functioning of certain glands. Such a nomenclature is useful clinically and we use it accordingly, but we must remember it only expresses but a part of the truth and sometimes that part may be a misleading one. It is no doubt that in the various degrees of myxœdema, for example, the thyreoid is primarily at fault; but the outstanding symptom which may bring the patient to the doctor, may point to the failure of some other gland. Misleading as it is to speak of underaction of a gland, it is often much more so to speak of overaction of any single gland. For example, in the case of the thyreoid, Graves's disease is often spoken of as synonymous with hyperthyreoidism. Although the thyreoid may be overactive in Graves's disease, it is so in common with the suprarenal, the pancreas, the thymus and probably others as well and the salient symptoms of the disease are due as much and perhaps more to the latter than to the thyreoid.

This question of interdependence of the endocrine glands must never be overlooked if we wish to get a clear conception of the many morbid manifestations which we have come to associate with inadequacy of any of the endocrine glands, but especially of the thyreoid. Of the thyreoid more than any of its congeners it may be asserted that when it fails to ring true, the others inevitably to some extent become jangled and out of tune.

HORMONE OF THE THYREOID GLAND.

The thyreoid gland is composed of closed vesicles embedded in areolar tissue, in the interspaces of which colloid is also seen and in which the vessels and lymphatics lie. The closed vesicles contain colloid material lined by a single layer of cubical epithelium without any basement membrane.

Although now ductless, the gland originally opened by the thyreo-glossal duct. The active principle or hormone of the thyreoid was isolated by Kendall of the Mayo Clinic. It is a crystalline substance rich in iodine (60% to 65% of iodine) to which he gave the name thyroxin. Kendall considered thyroxin was an iodine compound of indol, but it has now been shown by Harrington and Barger to be more closely related to tyrosin, containing four atoms of iodine attached to two linked benzene rings. It is therefore a body of comparatively simple composition and molecular weight. Kendall suggested that in Graves's disease this substance is formed without iodine in the molecule. The absorption of iodine by the thyreoid and its elaboration into the thyreoid hormone have been the subject of much investigation. According to Kendall the mode of action of thyroxin is to furnish the animal organism with ammonia resulting from the deaminization of the amino-acids. The amino-group in amino-acids is unavailable for the formation of urea and other nitrogenous compounds until it has been split out of the amino-acids. While this explanation which is based upon test tube analysis alone, may play some rôle in the various metabolic processes which the thyreoid certainly profoundly influences, it fails to account for various clinical phenomena. How, for instance, does it explain the striking increase in the absorption of oxygen varying from 20% to 75% when thyreoid is administered to patients with myxœdema or cretinism or the fact that thyreoid feeding will cause an increase of from 10% to 40% of oxygen intake in normal animals? How again does it explain the familiar increased elimination of phosphoric acid first observed by Chittenden in 1897 and that of phosphates which follows feeding normal animals with thyreoid and the great decrease in thyreoidectomized animals? Lastly, how does it account, if Kendall's view is the whole story, for the rapid reduction of fat in obese subjects taking thyreoid?

I would like to digress here for a moment to say a few words about the parathyreoids. Some years ago it was thought that the parathyreoids were mere accessory or supplementary or immature thyreoids, but it is now definitely known that they have a structure and function distinct from and even antagonistic to the thyreoid, that they are anabolic in function leading to the building up of calcium in the blood and nervous tissues and having a sedative action on the latter and that they probably cooperate with the internal secretion of the pancreas on the blood sugar. Like the thyreoid their secretion seems capable of being absorbed from the alimentary tract. Their action may be summed up by saying they have a very favourable influence upon calcium metabolism and on certain conditions of auto-intoxication. These glands seem to have a very definite part to play in the defensive mechanism with which the endocrine system and particularly the thyreoid as a whole is endowed. Parathyreoid extract has been used therapeutically for many conditions, but the best results appear to have been obtained in tetany, sprue, chilblains and chronic benign ulceration, both internal and external.

To return to the discussion on the probable action of thyroxin. Sajou's theory is that the thyreoid product, a compound of comparatively simple composition and molecular weight, rich in iodine, stimulates oxidation by increasing as a ferment the

[1] Read at a meeting of the Western Medical Association at Parkes, New South Wales, on February 15, 1928.

vulnerability of the phosphorus to oxidation by the oxygen of the blood. This process acting as well upon bacteria and on toxins upon which it acts as sensitizing substance or opsonin, favours their conversion into eliminable wastes by antibodies. This view explains the laboratory phenomena observed in practice, the excretion of phosphates and the intense oxidation both of which are phases of metabolism, the stimulation of the auto-defensive processes including phagocytic activity and finally the fact that thyreoid feeding provides or conversely that thyreoidectomy or thyreoid insufficiency inhibits all these functional phenomena.

However, inasmuch as Kendall's thyroxin has been found in as small a dose as ten milligrammes to increase the basal metabolic rate in myxœdema and cretinism and to produce symptoms of exophthalmic goître when given in excess, it bids fair not only to take the lead over all other active glandular agents so far isolated from the thyreoid, but to furnish in the near future a logical basis for all processes, physiological and pathological, concerning the gland, the chemical reaction so far submitted by Kendall being admittedly theoretical.

Of all the secretions formed by the body, as far as we know the thyreoid alone contains iodine and the colloid in the vesicles may be looked upon as containing a reserve of iodine for the body's needs and metabolism. When the supply falls short, this reserve supply is drawn on. As McCarrison puts it: "The thyroid is to the human body what the draught is to the fire." It stimulates growth in the young and is essential to the development of the fœtus. It assists in the destruction and elimination of the protein molecule, diminishes the storage of sugar and promotes the dehydration of fat. It also lowers the threshold of the response to sympathetic stimulation and consequently it is an active accelerator of metabolism.

Its close connexion with reproduction is shown by the physiological enlargement of the gland in the female at puberty, marriage and pregnancy and its partial involution at the climacteric.

Moreover, myxœdematous women seldom become pregnant and when they do in the absence of thyreoid medication they invariably abort. Very often the gland which may enlarge during pregnancy, will subside to some extent when the child is born, but the enlargement persists during lactation. These facts should be remembered when we are consulted about thyreoid enlargements, as they have an important bearing on the proper therapy and prognosis. In some women these prolonged calls of pregnancy have the effect of unduly exhausting the gland; they are unable to suckle the child, for lactation is dependent on a sufficient supply of thyreoid secretion. Such patients generally become obese and lethargic and they may remain so for varying periods until the thyreoid has had time to recover itself. When the iodine content of the thyreoid falls below 0·1% of its dried weight, the gland begins to enlarge. This occurs also as soon as three-quarters of the gland have been removed. Clearly, therefore, a considerable degree of iodine shortage has occurred before it manifests itself by thyreoid enlargement.

Puberty Goître.

In the transient goître of puberty the enlargement of the gland is due to an increased storage of colloid. The gland is called upon probably by gonad influence for an extra activity at this period of maximum body growth. Usually it responds without any signals of embarrassment, but in about 5% of females and a much smaller number of males the activity reaches a level higher than the requirements of the body demand and excess production is shown by thyreoid enlargement. This excess is stored up and hardly ever is there any sign of excessive secretion. It may be that the absence of any hyperthyreoidism and the evidence of storage are explained by the fact that the ordinary amount of iodine available is insufficient and this is supported by the fact that if we give iodine or thyreoid extract, these goîtres diminish in size. As a rule, however, they require no treatment; when the demand ceases, they subside and the stored colloid is elaborated and distributed. If they persist over the period of active growth, however, degenerative processes tend to supervene and the goîtrous swelling will then persist. The patients should, therefore, be kept under strict observation.

Endemic Goître.

Endemic goître usually starts in childhood or early life and in non-goîtrous districts it attacks females more frequently than males. Sporadic goîtres are less easily explained, but they appear more likely to occur in the children of hyperthyreoidic parents. The onset is usually insidious.

The thyreoid may undergo simple parenchymatous enlargement with or without increase of colloid or cystic degeneration. This includes the large group known as endemic goître. By far the most common type of endemic goître is the colloid goître and probably other anatomical types are due to degeneration processes in goîtres originally colloid. It is well known that endemic goître occurs in inland districts, particularly in certain districts generally much above sea level. The condition results from failure of the gland to elaborate its final product and to a resulting accumulation of imperfectly elaborated colloid. The accumulation is not related to any increased demand on the gland. It is surmized that the condition is due to a diet deficient in iodine. In this connexion I would like to refer to an admirable address given by Professor Hercus on the "Incidence, Ætiology and Prevention of Goître in New Zealand" at the last Australasian Medical Congress held in Dunedin. Professor Hercus deals with this subject brilliantly. Goître is a very serious though by no means a new problem in New Zealand and in parts of New Zealand it seems as prevalent proportionately as in Derbyshire and the high-lying Swiss valleys. In the first place he demonstrated that whatever may be the cause of goître, it operates independently of race. This was proved by exceedingly careful investigations carried out on the indigenous Maori and the European, 98%

of whom are of British stock in New Zealand. Unfortunately the Maori has to a great extent altered his habits of life to conform with that of the European and in consequence there is some evidence that the incidence of goître has increased. In an examination of one hundred and sixty-one Maori children in Canterbury, Professor Hercus found 14% with goître and in the Arewera country 30%. In the latter district he found the diet to be deficient in protein and fat and devoid of marine food. Members of the same tribe living in a river valley adjacent to the sea on a well-balanced diet in which shell fish appeared regularly, were found to be practically free from goître. Marine food and notably shell fish, both of which are rich in iodine, bulked largely in the diet of the Maori coastal tribes and this fact probably explains why tribes living on some endemic areas escaped the disease. He also shows that neither water nor calcium are primary factors. With regard to the former there are different sources of water supply, artesian waters, shallow waters, surface water and rain water in certain well defined endemic areas. Neither does Professor Hercus think that calcium can be an important ætiological factor, for the only pure limestone district in the endemic area of Canterbury shows a lower incidence of goître than elsewhere. At the same time its association in chalky districts, which has been noted in other parts of the world, may be explained not as used to be thought by the resulting hardness of the water, but by the permeability of the soil which readily allows of infection or contamination of the water supply as shown by McCarrison. Once established in a district it is apt to spread.

Although there is experimental evidence to show that, apart altogether from the iodine factor, diets containing excessive protein or excessive fat may produce thyreoid enlargement in animals, from evidence adduced Professor Hercus does not consider the question of diet an important one. Nor does he place much reliance on any toxic infective theories, either that there is a specific infective agent as the primary cause of goître or that the inhabitants of endemic areas have some specific intestinal flora, the toxic products of which either injure the gland directly or combine with the iodine in the food thus preventing its assimilation. Professor Hercus supports the theory that the disease is primarily due to deficient iodine intake. This he attempted to prove by a most careful investigation, firstly by examining the iodine content of the soil and secondly by a general survey of the iodine contents of foodstuffs. Regarding the former it was found that the amount of iodine in the soil bore an almost inverse relationship to the incidence of goître. The sea and basic igneous rocks constitute the principal reservoirs of iodine, although the actual iodine content of sea water is low, 0·023 grammes per litre. The quantity of iodine to be fom d in the soil derived from the rocks by weathering depends on the original iodine content, on the colloidal character of the soil and on the storage of iodine by plant life. There is a definite volatilization of iodine from the surface of the land and sea into the atmosphere. This atmospheric iodine is dissolved in rain water, snow and dew and thus returns to the soil. On examination of soils in New Zealand, it was found that endemic areas occurred where there was least iodine, that is areas where the soil was sedimentary, especially if sandy or gravelly, or areas that were drained from acid igneous rocks. On the other hand districts were remarkably free from goître where the soils were derived from or where drained from the basic igneous rocks and the nearer these approached the sea, the greater was the iodine content.

In connexion with the survey of the iodine content of foodstuffs, the foods richest in iodine are edible seaweed, sea fish, particularly shell fish eggs, wholemeal cereal products, leafy vegetables and milk. Refined cereal products, root vegetables and fruits have a low iodine content. The skin of root vegetables which is so constantly discarded before cooking, contains much of the iodine. Cooking was shown to have little effect on the reduction of the iodine content of seaweed, fish and root vegetables, but to reduce the content of green vegetables by about two-thirds, indicating the necessity for using the water in which green vegetables are cooked.

The iodine content of foodstuffs grown in typical goîtrous and non-goîtrous districts was investigated and it was seen that the foodstuffs of non-goîtrous areas contain much more iodine.

A most important fact to note is that iodine is distributed in such minute amounts throughout Nature that special methods of analysis are required to detect it. The unit of quantity is the microgramme which is one-millionth of a gramme or the equivalent of a micron in the linear scale. The cycle of iodine in Nature was first demonstrated by the work of Chatin in 1850 and his work has been confirmed and extended in recent years by Fellenberg.

The altered gland contains proportionately less iodine than the normal gland. It is unable to attach the required amount of iodine and the form in which the secretion can pass from the gland, is not reached to the normal extent. When the iodine content falls below 0·1% of its dried weight, the gland begins to enlarge. This occurs also as soon as three-quarters of the gland have been removed. Clearly, therefore, a considerable degree of iodine shortage has occurred before it manifests itself by thyreoid enlargement. The imperfect product, iodothyroglobulin, accumulates, distends the vesicles and so produces the goîtrous swelling. This interpretation is strongly supported by the fact that these patients are hypothyreoidic, their metabolism is unduly slow and their mentality usually more or less dull.

In support of Professor Hercus's views we know it is the rivers which wash soluble salts out of the earth and carry them down to the sea. Hence the sea becomes more salt at the expense of the land. Iodides are soluble salts and the effect of their removal naturally tells on the mountain valleys sooner than on the lowlands. Cretinism and goître

are much commoner in the former districts in various parts of the world and it is natural for us to ascribe such conditions as being due to iodine starvation. Hence there is strong evidence for the hypothesis that goître is caused by a deficiency of iodine and this may be probably one of the main ætiological factors, even though the matter is not quite so simple as this and may only be a portion of the true ætiological picture.

This naturally brings us to the question of prevention. The question has been dealt with especially in various parts of America by administering iodine in the public water supply and in the form of iodized table salt and iodized chocolate. Two kilograms of sodium iodide were added to every million litres (two pounds to 100,000 gallons) of water in the reservoir. Good results were reported from various parts and from Switzerland, but other observers have not had such favourable results and have actually found an increase in the incidence of goître. The method is one that is not a very practicable one and does not seem devoid of risk as it does not appear safe to administer iodine indiscriminately to children, many of whom are at the age of puberty. Moreover, it is always possible that iodine deficiency may not be the only factor concerned and as endemic goître was certainly commoner in past years in districts which had to depend solely on surface and well water at the time, it would not do for us to brush aside too lightly the theory of an infection having some bearing on the ætiology, even allowing the possibility of an iodine deficiency as well. Our main difficulty is that we have no exact method of calculating the exact amount of iodine deficiency that exists in a particular case. If we could overcome this our work would be much easier, but in any case very small amounts are necessary at all times.

Professor Hercus thinks that if practicable the most obvious method would be the raising of the iodine intake by the use of foods relatively rich in this element, especially edible seaweeds, of which there are various varieties in New Zealand, sea fish, shell fish, watercress, eggs, milk and green vegetables. In an endemic area, however, it is doubtful whether the measure alone would be sufficient as the initial deficiency lies in the soil and is reflected in the food product. This deficiency theoretically could be supplied by iodine manures of which there are several on the market, but the products are too variable to be reliable and so far not much headway has been made in this direction.

Two other methods of prophylaxis are the giving of iodine in medicinal form or the addition of iodine to some article of diet to the school children of an affected district. Both may eventually prove very valuable, but here again our difficulty is the question of dosage and the former scheme especially is open to serious objections. When it is remembered that the total iodine content of the normal adult thyreoid gland is approximately 30,000 microgrammes or 0·03 gramme (approximately a half of a grain), that the remainder of the body contains 1,000 microgrammes or 0·001 gramme (approximately one-sixtieth of a grain) and that the daily iodine requirement of the healthy gland is approximately 40 microgrammes only or 280 microgrammes weekly, it is apparent that excessive dosage may be easily used apart from the fact that we have no means of estimating the amount of deficiency for each gland at any time. All we know is that the amount required as an infinitesimal one. We must learn to think of iodine in terms of microgrammes and give it accordingly. I shall refer to this later in speaking of hyperthyreoidism.

The use of iodized salt has perhaps been attended with more satisfactory results and in the Swiss Canton of Appenzell am Rhein, where this measure has been adopted with proper precautions which include the prohibition of the sale of all antigoîtrous remedies, most of which contain iodine, the results have been remarkable. There the incidence of congenital goître has dropped from 50% to nil without any ill effects. In New Zealand the Department of Health introduced a definition of iodized salt into the *Food and Drugs Act* as being one part of potassium iodide in 250,000 parts of salt.

Considering the large and important issues involved and the harmlessness of the measure suggested, Professor Hercus is in favour of the compulsory iodizing of all cooking and table salt. This would supply the deficiency in a certain and physiological manner in the endemic areas and would not increase the iodine intake in non-endemic areas beyond one hundred microgrammes which Fellenberg has shown is the normal ingestion in some parts of Europe.

One thing is quite certain, that we should issue warnings to the public about the dangers involved in the indiscriminate use of iodine and especially of the great risks involved in using the many antigoîtrous remedies on the market, which are practically all preparations with varying amounts of iodine. The dangers that may arise from this, cannot be overestimated.

Simple goître is usually very chronic and in many cases produces no ill effects beyond disfigurement. Only those which appear rapidly, are likely to subside. Treatment must be as early as possible. If the basal metabolic rate estimations reveal that function is diminished, thyreoid extract is the best treatment and although some effect is produced by iodine dosage, thyreoid medication is more effectual, probably because the iodine exists here in a usable form. Either remedy is of service only in the early stages; goîtres of long standing are resistant to both on account of secondary changes, fibrous or cystic or both, when resolution is not possible. When these changes have occurred or the colloid goître persists, cosmetic consideration may indicate the only treatment which is the surgical remedy.

If the function is found to be normal or increased by estimations of the basal metabolic rate, iodine is the only remedy, but it must be given in very small and even infinitesimal doses and especially when function is increased it must be very cautiously administered, as in exophthalmic goître.

Adenomatous Goître.

After a simple goître existing for months or even years certain signs and symptoms of hyperthyreoidism may appear. The condition is known as toxæmic goître and usually occurs with multiple adenomata. The latter may be present either with or without signs of hyperthyreoidism and it is in this connexion especially that basal metabolic rate estimations are of the utmost value, inasmuch as if early removal is advocated for adenomata associated with hyperthyreoidic signs, the result will be dramatic, an immediate fall to normal of the basal metabolic rate and a complete disappearance of the hyperthyreoidic symptoms and signs.

There are three points in regard to these adenomata of much clinical interest. In the first place, many of the patients show signs of hyperthyreoid secretion and sympathetic excitation sooner or later, as in Graves's disease. Secondly, the adenoma is much less amenable to reduction by the use of thyreoid extract than endemic goître. Thirdly, in many instances iodine administration has been followed by hyperthyreoid symptoms in patients previously free from these symptoms and this intoxication once started may remain. Plummer says: "The administration of iodine for a few days or weeks to persons over thirty having adenomatous goître often initiates hyperthyroidism; once initiated this will continue for months or years." I shall have more to say about this later.

The explanation probably is that the iodine promotes the elaboration of the colloid into an absorbable form and the result is secretion by the gland much in excess of the body needs. Even without iodine these patients sooner or later show signs of hypersecretion; when the iodine becomes available, the sleeping mass is awakened into activity and the quiescent adenoma becomes active. They do not show the whole picture of Graves's disease, but they certainly show part of it.

Differentiation Between Toxic Adenoma and Graves's Disease.

Whereas in true exophthalmic goître the first symptom is usually exhaustion and nervous symptoms either precede or follow quickly on the thyreoid enlargement, there is always a considerable interval between the enlargement and the nervous symptoms in toxæmic goître. It is important especially to distinguish between the form of hyperthyreoidism occurring in Graves's or Basedow's disease and the hyperthyreoidism of toxic adenoma. Plummer in 1913 pointed out the chief differences between the two conditions. Whereas exophthalmic goître or Graves's disease has a rapid onset averaging nine to twelve months' duration and occurring most frequently in young persons, toxic adenoma is a chronic condition, averaging at least four years in onset and occurring as a rule in persons more than forty years of age. In exophthalmic goître as a rule the nervous symptoms, as already stated, generally precede or quickly follow on the thyreoid enlargement, while the symptoms of hyperthyreoidism progress by series of waves, at the crest of which all the symptoms are exaggerated and a crisis occurs. In toxic adenoma, on the other hand, there is always a considerable interval between the enlargement and the nervous symptoms which follow while the hyperthyreoidism progresses insidiously and slowly, causing a permanent damage to the heart, kidneys and other organs. In exophthalmic goître there is a rapid loss of weight and strength accompanied by a variable appetite which at times is ravenous. Likewise examination reveals exophthalmos in fully 50% of patients within three to six months of onset. The gland is symmetrically enlarged and thrills and bruits may be detected in fully 80% of the patients.

In patients with toxic adenomatous goîtres exophthalmos does not occur, the gland is asymmetrically enlarged; thrills and bruits are seldom noted. In toxic adenomatous goîtres, moreover, not only is there a slow development of the toxic symptoms, but there is usually a history of goître of years' duration, ten to sixteen or more.

Moreover, although the basal metabolic rate is increased in both conditions, the rate is usually considerably lower on an average in toxic adenomata, seldom rising above 50%, while in exophthalmic goître not infrequently rates of + 70% or + 80% and even higher up to + 100% are noted.

It has been said that hypertension occurs in the toxic adenomatous type of goître with a proportionately high diastolic pressure in contrast to a slightly elevated systolic and a relatively low diastolic pressure in exophthalmic goître, but it is a question whether this is a very reliable clinical sign in differentiating between the two conditions.

The importance of differentiating between the two conditions is obvious and the sooner this is done the better for the patient.

The adenomatous goître is the one form about which opinions are agreed as to the propriety of surgical treatment. If treated at all it should be treated surgically and this is especially desirable if the adenoma is single; it becomes a necessity if it is associated with hyperthyreoid symptoms. In this case surgical removal may be regarded as imperative and curative and the success is often astounding in the way the symptoms are completely relieved. The results are universally good. Diffuse enlargement with hyperthyreoidism is usually not adenomatous in nature and should be treated as exophthalmic goître.

Adenoma (*struma nodosa*) is not a hyperplasia or hyperplastic condition of the gland, but a true neoplasm. Cystic, hæmorrhagic, atheromatous and fibrous changes may all occur, which are phases of development and involution with degeneration. All these tumours arise from the ordinary thyreoid gland tissue and mainly from the epithelial proliferations in the centrally situated follicles of the thyreoid lobules and not from the fœtal rests (Aschoff).

Substernal Goître.

Substernal thyreoid enlargement is variously designated as intrathoracic, retrosternal and mediastinal goître or *struma profunda*. It is not so rare as is supposed. It is easily overlooked as it may be symptomless.

The condition is really an abnormal descent of the main gland, a lobe or an adenoma. Substernal thyreoid enlargement may be mobile, but more usually owing to its size or adhesions, it remains fixed within the chest.

The diagnosis of this condition is only possible by an accurate analysis of all the symptoms presented. They are of two distinct kinds: (i) Remote or toxic symptoms induced by hyperactivity of the gland or hyperthyreoidism, (ii) pressure symptoms resulting from mediastinal involvement and its adjacent structures.

The toxic effects may vary from a mild thyreoid hyperactivity to that of definite hyperthyreoidism with symptoms resembling very closely a fully established Graves's disease, yet without visible thyreoid enlargement in the neck. Frequently an obscure condition presenting only an auricular fibrillation of unknown origin in a heart apparently not diseased is due to a small goître that has had a tendency to extend down behind the sterno-clavicular joint or to an aberrant intrathoracic thyreoid. All such cases of auricular fibrillation of the type often designed as idiopathic, in the absence of the usual ætiological factors, should be carefully investigated as to the presence or absence of a substernal thyreoid. Any patient with symptoms suggesting thyreoid overactivity (rapid pulse, nervousness, irritability, debility and so forth) with signs of compression or intrathoracic pressure without any thyreoid enlargement or any patient with a visible goître and signs of compression alone should be investigated by means of the fluoroscope and Röntgen rays to determine the presence of an intrathoracic goître.

The main symptoms of compression are the usual clinical ones. The condition closely simulates asthma, chronic emphysema, aortic aneurysm, mediastinal and intrathoracic tumours generally and so on.

An important diagnostic factor is fixation of the trachea which may inhibit the normal excursion of the larynx. By placing the finger deeply in the suprasternal notch, one may feel a firm elastic mass rising with the larynx during coughing and swallowing, but with no palpable expansile pulsation characteristic of an aneurysm. Oliver's sign (tracheal tugging) is never present in substernal thyreoid, though the mass moves with the trachea during respiration.

It is remarkable how even fairly large intrathoracic goîtres may remain symptomless owing to the capacious thoracic cavity and mobility of its contents which occasionally may escape compression and so produce no symptoms or signs. An occasional symptom met with is hoarseness due to paresis of the vocal cords which in turn is caused by pressure or traction upon the recurrent laryngeal nerve.

Pain is never present unless the tumour is malignant.

As an aid to diagnosis in these cases bronchoscopy is not much help; it is dangerous and moreover does not give much idea of the position, size and type of the tumour. Even errors from X ray examination are possible, but only in regard to the type or pathology.

X ray examination frequently reveals the trachea to be compressed and deviated from normal. Substernal goître may be mistaken for a sacculated aneurysm of the ascending arch of the aorta, but fluoroscopy is very helpful in differentiating between these two conditions. If the shadow moves synchronously with the respiratory movements and lacks expansile characteristics, aneurysm can be eliminated definitely. Occasionally an aneurysm may lack expansile pulsation owing to firm clots in it, but in these cases the X ray plates if examined carefully will show a distinct line of demarcation between the shadow and the aorta. Persistent thymus infrequently seen in adults may be confused with substernal goître, but a persistent thymus is as a rule bilateral and has a more hazy and indistinct outline than other thoracic growths. Usually it does not attain the size of an intrathoracic goître and rarely, except in infants, gives rise to severe signs and symptoms of compression.

Hodgkin's disease and lymphosarcoma should not cause difficulty in diagnosis. They are situated at the lung hilus, spread peripherally like a butterfly, seldom have as distinct a margin as intrathoracic goîtres, are usually bilateral and often infiltrate the adjacent tissues. Moreover, the progress of these is more rapid and always downward.

Finally all tumours in the upper mediastinum in close proximity to the aorta should always arouse suspicion of a substernal goître, especially if X ray examination reveals a sharp, distinct and roundish outline and if they do not pulsate when viewed under the fluoroscope. An intelligent and complete fluoroscopic and radiographic examination of all patients presenting symptoms of so-called idiopathic auricular fibrillation, severe asthma, persistent cough and even aneurysm will usually suffice to diagnose a substernal thyreoid.

Treatment.

Very little can be said concerning the treatment of substernal goîtres, as many are symptomless and remain benign for years.

Small doses of iodide as used for control of goître in endemic regions may be useful, especially if the patients are seen early; they may then be controlled.

When symptoms of mediastinal compression are severe, recourse must be had to ordinary or deep X ray therapy which has been beneficial in a few reported cases, or surgical treatment which is probably the best and most reliable. At the same time, operative measures are attended by a good deal of risk and should be resorted to only when the symptoms are grave and have failed to respond

to more conservative methods of treatment. If surgery is decided on, it is probably better to operate without any previous X ray therapy of any kind, owing to the possibility of dense adhesions which would make any subsequent operation very much more difficult and dangerous.

Metaplastic Goître.

There is one other form of endemic goître that has been met with clinically which is worthy of mention; this is the form that has been called the metaplastic goître. It usually occurs in children between the ages of eight and fifteen years and is unlike the usual form of endemic goître in that the enlargement of the gland is entirely due to overgrowth of the epithelial element. In sections from these goîtres spaces packed with cells, some of the cuboid epithelium type, others of an unripe sarcoma-like type, are seen. This is why the first types described pathologically were thought to be sarcomatous, but this was later revised.

Patients with this type do not show the symptoms of Graves's disease, but there is usually tachycardia and this is generally aggravated by iodine dosage. The gland is consequently overactive without any definite disorder of function. It often occurs in families, while there are developmental and congenital influences.

Before proceeding to a discussion of the pathological conditions of the thyreoid associated with a loss or increase of function, that is, with hypothyreoidism or hyperthyreoidism, I wish to refer to basal metabolic rate estimations, the introduction of which into clinical work has given valuable results and much information.

Metabolism means the tissue utilization of food substances and as oxidation is involved mainly in this, metabolism is really a process of slow combustion. By basal metabolism is meant the amount of oxidation taking place in the body at complete rest and after a twelve-hour fast; in other words it is the energy expenditure of an individual at complete mental and physical rest. Clinically this is measured by the rate of the carbon dioxide production from the oxygen inhaled or since combustion is attended with exothermal chemical reactions, it may be measured by the amount of heat given out. There are therefore two methods of measuring metabolism, either by the heat given out or by the gaseous exchange in a given time.

To estimate the basal metabolic rate only the vital systems should be at work. Complete mental and physical relaxation is essential; to get accurate results the patient must be in bed and starved for at least twelve and even twenty-four hours. This will insure the metabolism being purely basal. The surface area of the person plays a very important part in basal metabolic determinations. The smaller the weight, the greater the area proportionately and hence the tissues will have to work at a greater rate to keep the area at a constant temperature. The smaller the animal, the higher is its metabolic rate and the greater the area, the more energy required to keep it at a constant temperature. The metabolic rate is usually expressed per square metre of body surface, either in calories or more usually clinically in cubic centimetres of oxygen per unit of time. Age and sex have a bearing on metabolic rates and allowance must therefore be made. When the metabolism has been calculated, the correct basal metabolism for a normal person is looked up in a table and the patient's result is expressed as a percentage increase or decrease. A range from – 10% to + 10% is looked upon as being within the normal range.

There are various methods of determining basal metabolic rates: (i) calorimetric and (ii) gasometric; the latter is further subdivided into (*a*) closed methods and (*b*) open methods. Of the first form one of the best known calorimeters is that at the Russel Sage Institute, New York, but it is very expensive. It is said that its accuracy is amazing.

Of the gasometric methods there are many examples of the closed, one of the best known being made by the Lanborn Company, of Boston. The principle of them all is the same, being a reservoir like a small gasometer with a water seal which is filled with oxygen, the patient inspiring oxygen through the mouthpiece and expiring through the soda-lime chamber into the reservoir again.

The most extensively used of the open methods in Great Britain at any rate is the Haldane apparatus, which consists of a canvas bag, known as the Douglas bag, provided with mouthpiece and valves and a Haldane gas analysis apparatus, together with a gas meter and sampling tubes.

The specimen from the bag is analysed. Although rather complicated, needing an expert to handle it, it is said to be a very accurate method.

One of the most important details is the preliminary treatment of the patient. He must be in bed and be starved for twelve to twenty-four hours to reduce his exogenous metabolism and glandular secretions to a minimum. The patient should neither read nor talk and as the slightest degree of apprehension may influence a result, all elements of fright or nervousness of the apparatus must be eliminated. Determinations should be made at the bedside, and if done in another room the patient should be wheeled there on a trolly and left there for an hour before the estimation is carried out.

Estimations should never be attempted with an ambulatory patient, as the results obtained are of very doubtful value.

For determinations to be of value and comparable, the same rigid conditions must be adhered to in all cases.

Interpretation of Results.

All agree that an error of + or – 10% or + or – 15% is possible. In the calorimetric methods the only source of error is the patient moving, which would increase his rate. Many factors may disturb a metabolic rate and in view of these, in using the Douglas bag method several estimations should be made on the same patient and continued until the results obtained agree within 5%. It is unwise to place too much reliance on a single determination as so many errors may creep in. In spite of these

troubles the estimations obtained are of the greatest value. By them valuable information is obtained showing endocrine disturbances especially of the thyreoid gland and pituitary body.

An increased metabolic rate is one of the main features of hyperthyreoidism, while a decreased rate is characteristic of hypothyreoidism. Consequently it is of very great assistance in distinguishing between goitres with increased and decreased thyreoid activity, that is between toxic and non-toxic goitres or adenomata.

Repeated basal metabolic estimations give the most accurate information as to progress and help to decide when medical therapy has reached its limit. Many Americans rely solely on the basal metabolic rate determinations for indications for surgical treatment, but others think the cardiac side of the disease and the blood pressure are just as important and they rely upon the clinical and electrocardiographic examination as well as the metabolic for indications as to treatment. Most people think that if the basal metabolic rate keeps over 30% after a proper medical therapy, operative intervention is called for, while extensive operative interference is unwise when the basal metabolic rate is over 50% and even over 40% increase.

On the other hand in conditions of hypothyreoidism such as myxœdema, the rate is decreased down to 20% to 40% below normal and even more. This rate can be restored by administration of thyreoid extract and repeated estimations will show the rate of improvement and so check up accurate dosage of thyreoid extract. As the thyreoid is the main activator of metabolism, disturbances of the other endocrine glands do not produce such comparable changes, but prolonged undernutrition, terminal stages of chronic nephritis, diabetes and particularly hypopituitrism are all associated with a decreased basal metabolic rate. In conditions associated with hypopituitrism the decrease is usually not much greater than −15% to −30%. That this is not due to an associated lowered thyreoid function can be determined only by clinical examination or by noting the effects of an injection of pituitrin which should be followed by an immediate increase in the basal metabolic rate if the pituitary is at fault and which increase will not occur if the thyreoid alone is at fault. Nevertheless in many of these patients there is some associated thyreoid underactivity. In pituitary overaction the rate is usually raised and here again there is probably some combined thyreoid overaction.

Before dismissing this subject, I would like to refer to a formula known as Read's formula, for calculating the basal metabolic rate in hyperthyreoidism. Read found that by estimating the pulse rate and pulse pressure under basal conditions, the rate could be calculated with an error of only 10% in 60% of patients and of 20% in 91%. The error may be a *plus* or *minus* one.

The formula is as follows:

$$B.M.R. = 0{\cdot}683\ (P.R. + 0{\cdot}9\ P.P.) - 71{\cdot}5$$

where P.R. = basal pulse rate and P.P. = basal pulse pressure, that is the difference between the systolic and diastolic pressures when the patient is kept under basal conditions.

Experience of this formula by several authorities has shown that it corresponds fairly closely with accurate basal metabolic rate determinations and consequently it is useful when it is not possible to get accurate basal metabolic rate estimations carried out.

Conditions Associated with Hypothyreoidism and Diminished Function.

The commonest pathological conditions associated with diminished function of the thyreoid are myxœdema and cretinism, but it is just as important from a clinical point of view for us to recognize minor degrees of thyreoid insufficiency. The cause of overaction is generally a toxæmia which may irritate many glands though in a different degree. Long continued toxæmia, however, may also cause underaction owing to the fact that it may lead to exhaustion of the gland. This is seen in thyreoid deficiency as apart from being the main activator of metabolism in the body, the thyreoid's second great rôle is to act as one of the main defences of the body and is concerned in combating endogenous toxins. In a somewhat lesser degree long continued toxæmia may lead to pituitary insufficiency, but we must remember that the main question in endocrine medicine is one of balance, some of the secretions being synergistic and some definitely antagonistic to others.

Myxœdema.

The remarkable interdependence of the endocrine glands is further borne out by the close resemblance of many symptoms and often with their practical identity. With thyreoid or pituitary deficiency we associate adiposity, infantilism, mental hebetude and dulness, subnormal temperatures and slow pulse, hairlessness, somnolence, skin pigmentation. So, too, in adrenal insufficiency we see some of them, such as the hairlessness, infantilism, low temperature and pigmentation, though there is never adiposity; the change, if any, is towards emaciation. Consequently when one gland is at fault and deficient, the mere upset in the endocrine balance is sufficient to produce a characteristic set of symptoms referred to as the pluriglandular syndrome. At times, however, it is possible to tell which gland is primarily at fault. We can do so with the thyreoid for there are many clinical manifestations to betoken this, such as skin troubles, slow pulse, sensitiveness to cold, muscular fatigue, intestinal stasis, menstrual disturbances and in children adenoids, night terrors and nocturnal enuresis. Hertoghe, of Antwerp, was the first to point out that all these symptoms might be produced by some material infiltrating various organs. The thyreoid is the great accelerator of metabolism and when it is sluggish a product of inadequate metabolism is deposited in various tissues.

To detect minor degrees of thyreoid insufficiency one must always be on the alert and not allow the

importance of apparently trivial symptoms to escape one's observation.

The thyreoid secretion is essential to the fœtus. During pregnancy the thyreoid enlarges. Unsatisfactory babies are often the subjects of thyreoid deficiency, apart from well-known causes like syphilis and tuberculosis. In older children there is much to be said of the view that even if thyreoid insufficiency is not responsible for all the symptoms of the body in rickets, certain of its most salient features are, especially the bony phenomena. It is well known that the thyreoid secretion acting in conjunction with the parathyreoids is essential to the full utilization of the calcium salts and consequently when deficient in a growing young child we are liable to get inadequate osseous development. Clinically we know also that even though this is due to a relative absence of calcium salts, the administration of the latter even in large quantities has no effect in arresting the disease.

As the child grows older, if deficient in thyreoid secretion, he or she may become subject to night terrors. How it acts is uncertain, but this symptom disappears with judicious administration of thyreoid extract if given early enough. Nocturnal enuresis may be caused by thyreoid insufficiency and may be similarly cured. In this connexion we know how common is the association between adenoids and either nocturnal enuresis or frightstarts and how it is important that the first be removed for the cure of either of the two latter conditions apart from any other therapy adopted.

Enlarged lymphatic glands are often due to thyreoid inadequacy. They are usually seen in weakly children. They are usually situated at the angle of the jaw, may be hard, are not tender and show no tendency to suppurate. In this connexion we must be quite sure of our ground before administering thyreoid extract, because most tuberculous people stand thyreoid administration very badly and if the glands are tuberculous, much harm may be done.

I have referred to the fact that the internal secretion of the thyreoid constitutes one of the main defences of the organism against microbic invasion, for not only are subthyreoidic children less resistant to disease, but the occurrence of some infectious disease in a previously healthy child very often proves the starting point of troubles due to thyreoid inadequacy. The resistance to the poison makes a heavy demand on the gland and very often the latter may become exhausted or depressed only in function, even though only temporarily.

I shall now consider some of the main signs and symptoms which would lead us to conclude a person is subthyreoidic. Among the most important are a subnormal temperature, the eyebrow sign or *signe de sourcil*, carious and irregular teeth, premature greyness of the hair and baldness, abnormalities of pigmentation, certain skin lesions, the so-called obesity of the subthyreoidic and slowing of the pulse.

When thyreoid administration is successful the temperature becomes normal; if too much thyreoid is being administered, it may rise slightly above normal.

The eyebrow sign or *signe de sourcil* was first described by Hertoghe, of Antwerp. It consists of a scarcity or even a complete absence of hair of the outer two-thirds of the eyebrow. This sign is by no means invariable, but is very suggestive, while on the other hand very perfect eyebrows can exist with definite thyreoid inadequacy.

Some abnormalities of cutaneous pigmentation, especially leucodermia, are common in all thyreoid disturbances whether of underaction or overaction and though it would be foolish to regard them as pathognomonic, their presence may be of value as additional evidence when combined with other more or less distinctive features.

Grosser forms of skin affections as psoriasis and eczema and even ichthyosis as well as milder forms such as urticaria and transitory œdemas affecting the deeper structures, are often associated with thyreoid insufficiency.

The so-called obesity of the subthyreoidic is not a true obesity, it is more of the nature of an adiposity. In the very earliest degree it shows itself as a very slight deposit of myxœdematous tissue under the skin more noticeable in certain parts, for example, the area over the deltoid and upper part of the trapezius. In women the parts just below the breasts may show the same characteristics. When more pronounced the deposit again favours certain regions, for example, over the seventh cervical vertebra, so that a patient who is really upright, appears to stoop. This may attain the size of a closed fist and has a hard consistency quite unlike ordinary fatty tissue. Other regions include the areas over the deltoid, over the triceps and over the walls of the abdomen. In women and to a much less extent in men the region immediately below the breasts is generally covered by a deposit of myxœdematous tissue; often rolls of it can easily be mistaken for true fat; the breasts themselves are often relatively small, though they are apt to be hard and firm. In women, however, perhaps the most noticeable and conspicuous deposits take place in the gluteal region.

Subthyreoidic people like those with myxœdema usually have a somewhat slow pulse. They tend to be hairless or the distribution of hair is usually scanty. They are somnolent and there is mental hebetude. Their brains move slowly; they are apt to be forgetful. They will meander along in conversation about irrelevant matters, but are curiously reticent about themselves; they have therefore to be closely questioned about purely subjective matters. They are unduly sensitive to cold, they have great difficulty in concentrating on any subject; their memories are very unreliable, especially for small things. General asthenia, fatigue, muscular and mental, are always present in a greater or less degree, but this again has to be found out by questioning; the information is usually not volunteered.

Most, if not all, of the above symptoms characteristic or suggestive of hypothyreoidism are explicable if we remember that material that should be

catabolized, may cause infiltration of tissues. Thus infiltration of the Eustachian tubes and accessory sinuses may cause headache, giddiness and somnolence; infiltration of fasciæ and ligaments may produce rheumatic manifestations, even knock-knee, painful heel, flat-foot and lordosis. There is evidence, moreover, that true rheumatism flourishes best on a subthyreoidic soil. Nocturnal enuresis in these cases is probably due to some desquamation of the bladder epithelium rendering it more irritable. Infiltration of the nerve centres causes the mental slowness and loss of memory.

When the deficiency becomes great, the condition approaches more or less to a true myxœdema. In these patients the skin becomes harsh and dry, the hair becomes scantier, the eyelids get baggy, supra-clavicular pads of fat develope, to be followed by deposits of tissue closely resembling fat in other parts of the body. The hands may become thick and spade-like; the legs swell but do not pit on pressure. Constipation is the rule and may be very obstinate. There is a tendency to amenorrhœa, though menorrhagia may occur. The basal metabolic rate may be reduced by 40% or more and the temperature is subnormal. The symptoms are aggravated in cold weather as one would expect and the liability of hypothyreoidic individuals to chilblains is well known, while a condition resembling Raynaud's disease is not uncommon. Many of these people have a definite visceroptosis with which often is associated an intestinal toxæmia which further exhausts the thyreoid and so establishes a vicious cycle. Myxœdema is so well known that I do not propose to discuss it in further detail.

Cretinism.

Cretinism is due to a congenital thyreoid insufficiency and is common in goîtrous people or in the offspring of goîtrous or hypothyreoidic people and consequently it may be endemic or sporadic. The growth is stunted, there is delayed ossification of the bones, the nose is flat, the nostrils large, the hair thin and the general appearance at once recalls myxœdema. The tongue is large and often protrudes. The thyreoid is apt to be goîtrous. Sexual and mental development are much retarded; the disposition is placid. If treatment is to be at all successful, it must be adopted very early.

In all cases of cretinism there are early and destructive changes in the gland. It is interesting to note the opinion in Switzerland with regard to this disease. It seems to be the accepted idea that there is no treatment for the established cretin state and that much was hoped from the addition of iodine to the general dietary of the country in the form of iodized salt. This seems to bear out that medical authorities of Switzerland, where endemic goître is so prevalent in parts, accept the view that iodine defect in the diet leads to a functionless and degenerated gland with secondary changes which virtually destroy it. Beyond the stunted growth, the chief characteristic of the cretin is his idiocy; he is infant-like in his cerebration, will work when he is set some simple task and is watched at it, has maudlin and amorous habits and smiles and chuckles at his own ideas, if he can be said to have any.

Treatment often has to be prolonged, while in fully developed myxœdema the administration of thyreoid has to be kept on indefinitely; the patient after a short time gets to know the exact dose that suits him best. Each patient has to be treated on his own individual merits, but it will be helpful in our therapy if we understand clearly how thyreoid extract is best administered and especially the symptoms that may arise when our dose is in excess of the patient's needs.

Thyreoid Medication.

In a matter of dosage it is better and safer always to prescribe thyreoid in terms of the fresh extract, for *thyreoideum siccum* is five times as strong and this does not admit of such a ready variation in dosage and moreover minimizes the risk of overdosage.

Many reliable preparations are available.

The dose of the fresh thyreoid extract is quoted in most textbooks at 0·18 to 0·6 gramme (three to ten grains) three times daily, the last a dose so large that it would be ludicrous were it not so dangerous. The proper dose is from five to six milligrammes to six or at most twelve centigrammes three times daily. With the exception of certain types of lunatics, it is only the most robust among the healthy who can take large doses with impunity, unless these larger doses have been arrived at progressively from very small beginnings. There is one important fact which the prescriber of thyreoid should ever remember: the more a patient requires the drug, the smaller will be the initial dose he will tolerate.

Having ascertained by cautious and slow increase from small beginnings the dose best suited to each patient, the dose is continued for three weeks. It is then suspended for a week and resumed for three weeks and so on. If the pulse rate is not slow from the first from some extraneous cause or if there is any other factor that may indicate intolerance, the drug may be given for a fortnight and suspended for a fortnight.

Thyreoid medication may occasionally, but by no means always, regulate the bowels. The stools of those taking the drug generally become very light in colour.

When it is acting satisfactorily in hypothyreoidism of moderate degree, thyreoid medication increases the urinary output. The patient should have the urine tested once a week at least, as although the occasional presence of albumin in the urine need not excite alarm, the appearance of sugar should always lead to a suspension of the drug for the time being. True diabetes has been said to have followed myxœdema after many years, but this must be very rare.

If the best results are to be obtained from the thyreoid medication, the ordinary mixed diets require some slight modification. Starchy foods (carbohydrates) should be very sparingly taken, while sugars (sweets, lollies, chocolates and sugar

itself) should be eliminated as completely as possible. Common salt also should be eliminated from the dietary as an extra article of food, though the small amounts used in the cooking of all ordinary articles of food may be allowed.

Alcoholic drinks should be very moderately taken, if at all, while thyreoid is being administered.

The introduction of tablets as a means of exhibiting even organic substances has made the administration of thyreoid to older children easy; for an infant tablets are, of course, unsuitable, but crushed and given as a powder they are convenient at this age also. In very young infants eight milligrammes gradually working up to three centigrammes of the thyreoid extract in the form of a tablet crushed into a powder would probably be a sufficient dose. After a week or two if necessary, this may be increased to six centigrammes. The younger the child the greater the necessity for caution. The main symptoms of ill effect seen in children are irritability of temper, excessive loss of weight, faintness, headache, rapidity of pulse, nausea and fever. Should any of these supervene, the drug should be suspended at once and resumed later.

As long as the weight of the child is increasing, the drug may be continued, but as soon as the weight becomes stationary, the drug should be suspended and if the weight decreases, the drug must be discontinued.

In the case of children other than cretins and children who are over normal weight as a result of abnormal function of some other gland, the body weight is a useful indication of the effect of the treatment.

Pathological Conditions of the Thyreoid Associated with Hypersecretion.

Hyperthyreoidism or hyperthyreoidia is a condition which is due to toxæmia of focal, systemic or neurogenic origin which by provoking a definite reaction of the thyreoid apparatus causes it under certain circumstances to secrete its physiological hormone in excess, thus provoking in all tissues including the nervous system correspondingly active and destructive katabolism. It is probable that hyperthyreoidic conditions, including Graves's disease, are produced by the combined effects of toxic and psychic factors. Not all cases of overactivity of the gland go on to true Graves's disease.

The main pathological conditions of the thyreoid associated with hypersecretion and increased function are conditions of thyrotoxicosis clinically demonstrated by a toxic goître or a toxic adenoma, simple hyperthyreoidism without the typical symptoms and signs of Graves's disease, Graves's or Basedow's disease, often referred to clinically as exophthalmic goître.

Graves's Disease.

Ætiology and Pathogenesis.

Whether Graves's disease is a dysthyreoidism or simply an expression of pure hyperthyreoidism or of hyperthyreoidism associated with other endocrine disturbances, in the light of our present knowledge it is no longer necessary to defend the view that in this disease there is an excessive activity of the thyreoid. So solidly based is this fact on both clinical and experimental data that many authorities urge that the term hyperthyreoidism or its more correct synonym hyperthyreoidia implies that the clinical entity of Graves's disease is present. Its adoption, moreover, is all the more warranted in that it does not entail elimination of the nervous theory long deemed by many to be the main one, since the sympathetic system is involved. Nor can the thyreo-genital, the thyreo-hypophyseal, the thyreo-thymic, the thyreo-pancreato-adrenal nor even the neuro-thyreo-adrenal theories be set aside, since each one of the organs in the various designations can be shown to participate more or less actively or passively in the pathology of the disease. Even Thomson's theory that the disease is due to intestinal auto-intoxication, with the thyreoid taking little if any part in the process, has contributed its share to our knowledge. We know that enlargement of the gland is not a necessary accompaniment of the excessive secretory activity of the thyreoid and that hyperthyreoidia may be caused not only by intestinal auto-intoxication, but also by a multitude of poisons both inorganic and organic, including bacterial toxins and fatigue waste products.

Toxæmia Genesis of Hyperthyreoidism.

It is probable that any toxæmia, especially if prolonged, excites the functional activity of the thyreoid gland and that this is more or less developed according to the virulence of the toxæmia. The fact that the antitoxic and bactericidal resources of the body are largely dependent on the functional activity and perfection of the thyreo-parathyreoid mechanism is probably as well established as is the influence of this mechanism on metabolism. The thyreoid gland, apart from being the main activator and accelerator of metabolism in the human body, is one of our main defence forces in protecting the body when attacked by an infection. Sajou's hypothesis of the function of the thyreo-parathyreoid mechanism being the chief defence against infection has been confirmed clinically and experimentally; it affords the keystone upon which the rational treatment depends. The well-known acceleration of the metabolic rate brought about by thyreoid gland administration is at the same time the process through which the protective power is exercised, precisely as thyreoid is known to break down, that is to katabolize fats, so it also breaks down and katabolizes many varieties of bacteria, their toxins and other poisonous substances. It has never been maintained that the protective function referred to was a universal phenomenon against all forms of intoxication. What is claimed is that only bacterial toxins or other poisons, organic or inorganic, which are capable of acting as antigens, are also capable of provoking thyreoid hypersecretion.

Practically all the febrile infections have been known to cause hyperthyreoidism with typical histological lesions in the thyreoid denoting exces-

sive functional activity and proliferation of glandular tissue. This applies also for various poisons, wastes, toxins and detritus associated with intestinal stasis, septic foci or processes and various auto-intoxications. Any of the foregoing disorders which assume chronicity, tend to predispose individuals to bring about and sustain the thyreoidal morbid process. Chronic infections of nasal sinuses, the naso-pharyngeal space and particularly of tonsils after repeated attacks of tonsillitis are often encountered. The tonsillar infections, pyorrhœa, carious teeth, apical abscesses may greatly predominate in the causation of a condition of hyperthyreoidism or of the Graves's syndrome. In fact the condition, if only in a comparatively early stage, often disappears after removal of the causative infection. This applies likewise to coprostasis; when adequate measures are resorted to, in order to eliminate the fæcal masses, the pathogenic toxæmia disappears.

The septic foci are most often to be found in the naso-pharynx, particularly in the tonsils, though the antra or accessory sinuses may be responsible. Next to tonsillar infections, dental sepsis is commonest. The clinical lesson to be learnt from this is that in hyperthyreoidism, early or late, including cases of Graves's disease, we must search the body for any demonstrable foci of infection, paying particular attention to the teeth and tonsils. Whether a toxic focus results in hyperthyreoidism or Graves's disease or not, depends largely on many factors, especially the emotional state.

Psychoneural Genesis.

Fright, particularly if accompanied by traumatism, may be a prominent cause of thyreoid hyperactivity, though fright alone may suffice. In addition a sudden shock or any prolonged strain on the emotional nervous system must lead to overstimulation of the thyreoid especially in people who exercise great self-control. This was well seen after the air raids in London and the San Francisco earthquakes, when many self-controlled people unconsciously diverted their impulses to the vegetative system. The result was that a large number of persons became affected with hyperthyreoidism and Graves's disease. That fright or sudden shock may cause Graves's disease forms one of the strongholds of the nervous theory. Indeed the symptoms of intense fright and Graves's disease are similar. What is the underlying cause of this similarity? How can so remote a cause or factor as fright, deep grief, anger or many other similar conditions in which the emotions are violently stirred, awaken the same morbid process in the thyreoid as do a multitude of poisons and thus cause excessive functional activity? It is found on analysis that a toxin acts as the pathogenic factor.

Briefly, fright or anger may bring about disintegration of the nerve cell by subjecting it to violent stimulation which means excessive metabolic activity. Excessive metabolism of the nerve cell is known to produce phosphoric acid, cholin and also especially a substance closely allied to muscarin and known to be very poisonous, neurin. So sensitive is the thyreoid to this that it was once believed that the one function of the thyreoid was to destroy neurin as fast as it was formed. In the light of these facts it can be realized that a poison, even though neurogenic in origin, may become the primary cause of the disease. But why, once the excessive stress due to fear is ended, does the morbid process continue? Why do all the morbid processes, particularly those of nervous origin, persist? This is due to a vicious cycle. The thyreoid, powerfully stimulated to react against the intoxication itself, actually becomes a destroyer of the nerve cell. This becomes intelligible when we recall that besides containing chromatin, the nerve cell is likewise rich in fatty substances, lecithin (containing oleic, palmitic or stearic acid) in particular. If we also recall the familiar fact that the thyreoid gland first attacks fats, breaking them down sooner than it does any other tissue, we realize why it is that excessive thyreoid activity disturbs the nervous system. A severe mental stress causes excessive katabolism in the nerve cells and the excretion of highly toxic waste products including neurin; these poisons by provoking a defensive reaction of the thyreoid, cause it to break down fats including the fatty components of the nerve cells, thus establishing a vicious cycle by perpetuating the katabolism of these and the formation of poisons. This accounts for the severity of such cases unless they are treated in some satisfactory way to arrest excessive thyreoid activity. It accounts, moreover, for the well-founded contention that exophthalmic goître is a nervous disease. Hyperthyreoidism and Graves's disease are probably due primarily to some toxin originating from a pathological process in one or more organs, either tonsils, teeth, gums, accessory sinuses, stomach, intestines or genito-urinary organs or to some toxin formed in the cerebro-spinal neurones subjected to stress. Any one of these poisons further excites the thyreoid apparatus to supranormal activity, owing to the active part taken by the apparatus in defensive functions. The thyreoid hormone being thus produced in excess, breaks down not only fats throughout the body at large, but also the fatty bodies in the nerve and brain cells. In all cases, therefore, whatever their origin, destructive nerve tissue katabolism occurs. When we remember how closely all the endocrine glands are connected and how the thyreoid disturbance is apt to produce disturbances in function in many of the other glands, it is quite easy to account for all the nervous phenomena that occur in hyperthyreoidia and Graves's disease, while the excessive katabolism explains the emaciation which is often rapid and extreme. To the neurogenic wastes thus produced must be added the waste products of all other tissues subjected to excessive katabolic activity by the overacting thyreoid, while these wastes goad the latter to still further activity.

Hyperthyreoidism is thus seen to be the product of a vicious cycle in which three classes of poisons take part: The primary causative poison which

excites the thyreoid apparatus, the excess of thyreoid hormone which provokes excessive katabolism in all tissues including the cerebro-spinal and peripheral nervous systems, excess of katabolic wastes, derived from all tissues including the nervous tissues.

At the same time there must be some predisposing influences as well, as only a small proportion of people exposed develope exophthalmic goître. The latter may occur as a complication of small goîtres which had previously caused no trouble after a period of overwork, intoxications, dysentery, typhoid, violent emotions and long-continued anxiety. Many instances of this kind were seen during the war. This will also account for the relative frequency of Graves's disease in goîtrous districts and emphasizes the close connexion between the two conditions. There are some tests that will yield evidence that some cases of apparently simple goître later have to be placed in the hyperthyreoidism class as a result of one of the many sources of toxæmia. In the larger class in which no goître exists as a starting point, the history usually shows that some disease of childhood, diphtheria, measles, scarlet fever in particular, has caused focal lesions in the thyreoid which by forming sclerotic areas have diminished its functional efficiency. The organ, under the stress of some chronic infection, is then unable to carry on its functions adequately without becoming inordinately hyperæmic, an abnormal process which entails the formation of adventitious vessels and tissues, that is the pathological lesions characteristic of hyperthyreoidism. In all such cases, therefore, the predisposing influence is an acquired thyreoid insufficiency.

Graves's disease occurs at all ages and in all parts of the world, though the incidence seems to be greater in goître districts. It is more frequent in females in the proportion of between nine and eleven to one. It is prone to run in a cyclic course with remissions of recrudescences and has a tendency towards chronicity, though it may result in a spontaneous recovery. The most constant feature of this disease without which the diagnosis is never justified, is an elevated basal metabolic rate. When accurately determined, it furnishes a reliable objective, quantitative estimate of the severity of the disease and of any progress made with treatment.

The changes the heart undergoes in Graves's disease include tachycardia, with a rate of from 120 to 200 per minute, leading to myocardial exhaustion associated with atonia and relative valve incompetence. Dilatation occurs and the cardiac dulness is increased. The apex beat lies outside the nipple line. Epigastric pulsation is present and there is a pericardial basal rub. The sense of cardiac oppression and often præcordial pain is evident. Myocardial degeneration is encountered, especially when the condition has been present for a considerable time. The conductivity is impaired. Auricular fibrillation ushers in the stage of cardiac failure; this stage terminates in death.

The epigastric or episternal pulsation is not expansile and heaving as in aneurysm. Other associated signs are capillary pulsation, venous pulse in the hands, vascular erythema of the face and neck and other parts; throbbing pulsation of the arteries felt in the finger tips.

Auricular fibrillation may occur in Graves's disease under different conditions. It is often preceded in the various stages by the occurrence of frequent premature contractions which are of the nature of fatigue extra-systoles and indicate an exhaustion of the myocardium. Auricular fibrillation may be preoperative or postoperative. Preoperative fibrillations may be toxic or degenerative.

In postoperative cases, especially before the use of iodine as preliminary treatment for operative measures, fibrillations are prone to occur for twenty-four hours or longer after operation. It is for these patients that quinidine is most useful and should be used unless there is some definite contraindication.

The course of Graves's disease is very variable. Patients with mild forms generally do well under appropriate treatment. Probably about half recover more or less completely, but symptoms of thyreoid exhaustion may appear subsequently in some, so that a condition not unlike myxœdema developes. In others the disease becomes chronic and may lead to insanity. True diabetes may occur. Auricular fibrillation, diarrhœa and exhaustion are the commonest causes of death.

At some time improvement asserts itself in every patient, usually in early stages and though slight at first, it becomes so pronounced that the patient concludes that he is approaching full recovery. The tachycardia lessens, the tremors, irritability, emotionalism, heat flushes all tend to disappear, the emaciation is replaced by a relative *embonpoint*, the flattened breasts fill out and even the goître seems to recede.

Careful examination reveals, however, that the goître is no longer so compressible and here and there palpation will reveal nodular masses; the whirring sound over the gland is hardly audible and the character of the gland seems to have changed. Briefly, sclerotic areas are developing and connective tissue is gradually replacing the functional elements. Finally, cirrhotic changes progress sufficiently not only to reduce the secretion of the gland to normal, when the improvement and period of fictitious recovery ensues, but to decrease steadily until hyperthyreoidism may be replaced by hypothyreoidism and then by myxœdema.

Certain symptoms of myxœdema may appear before those of Graves's disease have completely disappeared. The early œdema which is sometimes seen in Graves's disease, and which does not yield to thyreoid medication, the loss of hair and other symptoms due to the katabolic action of the excessive thyreoid secretion, may be mistaken for those of myxœdema, though the signs and symptoms of the two conditions are quite different.

Myxœdema as a terminal stage of Graves's disease is far more severe than the primary form, as it seizes upon an already worn out organism. If the

patient does not become a prey of an intercurrent disease, he lapses into a profound cachexia with increasing cardiac weakness, mental torpor, alternating with periods of insanity of a degenerative type, soon followed by fainting spells and heart failure, which is the usual mode of death.

Apart from observation of the signs and symptoms of hyperthyreoidism typically seen in Graves's disease, there are some additional methods of investigating the condition of a patient in whom overactivity of the gland is suspected. There are many clinical tests of more or less value in common use for determining if a condition of hyperthyreoidism is present or not, but perhaps three deserve special mention: (i) Basal metabolic rate determinations (including the use of Read's formula) for calculating the basal metabolism in hyperthyreoidism; (ii) Loewi's mydriasis test and (iii) Goetsch's skin test.

All persons suspected of being affected by hyperthyreoidism should be kept at rest in bed and carefully studied. Some authorities use the thyreoid therapeutic test and give six to twelve centigrammes of thyreoid which would at once increase the symptoms and pulse rate in the presence of hyperthyreoidism. This, however, is a very risky and dangerous method of diagnosis.

I have already discussed the importance of the basal metabolic rate which is always raised in persons with hyperthyreoidic lesions.

Loewi's Mydriasis or Adrenalin Eye Test.

In hyperthyreoidism the sympathetic nervous system is abnormally irritable and the dilator fibres of the iris governed by the sympathetic system respond abnormally to adrenalin (epinephrin). Loewi found that in pancreatectomized animals, in human diabetes when the pancreas was at fault and in hyperthyreoidism, the instillation of one or two drops of a 1‰ solution of adrenalin chloride into the conjunctival sac and one or two drops five minutes later will dilate the pupil in from twenty minutes to one hour. When adrenalin is instilled into an excised eye, the pupil dilates, but normally this mydriasis does not occur with the eye *in situ*. In both hyperthyreoidism and inadequacy of the pancreas the response to the test is positive, the increased suprarenal action stimulating the sympathetic to excess. In the case of the pancreas the test is based on an upset in the normal antagonistic actions of the suprarenals and the pancreas. If the latter is in defect, the former will be relatively in excess and the addition of adrenalin will enable it to assert itself in both cases, so that dilatation of the pupil is no longer inhibited. In the case of hyperthyreoidism the sympathetic is in a state of increased irritability and the dilator fibres of the iris governed by the sympathetic respond abnormally to the action of the epinephrin.

Langdon Brown's experience of the test is that it is if anything too sensitive. The primary disease may be in the liver and the pancreas secondarily involved, yet the reaction may take place. Even so, the test, especially as an adjunct with other sources of information, is of the greatest value in the diagnosis of hyperthyreoidism.

The Goetsch Test for Hyperthyreoidism.

One half of a cubic centimetre of a 1‰ solution of adrenalin hydrochloride diluted with an equal quantity of sterile water is injected hypodermically into the arm, usually over the deltoid. The test is based on the fact that in hyperthyreoidism the patient is believed to be unduly responsive to adrenalin injections as the result of the thyreoid secretion sensitizing the sympathetic nervous system. The patient should be at rest in bed for at least two and preferably twenty-four hours previously and he should be assured that no danger or pain is involved in the test.

A reaction is recognized by the following characteristics. A rise within five minutes of the systolic blood pressure of ten to fifty millimetres of mercury. An increase in pulse rate with perhaps palpitation of the heart. The increase in pulse rate varies from ten to fifty beats and is usually over twenty per minute, the increase being usually proportional to the degree of intoxication present. With the early rise of the systolic blood pressure, there is also an early fall of the diastolic pressure of about ten millimetres of mercury. After about half an hour the pulse and systolic pressure fall somewhat and this is followed by a secondary rise of both to a less degree. In about one and a half hours the blood pressure and pulse rate have returned to their initial levels. Usually symptoms of hyperthyreoidism present before the injection are exaggerated, such as tremors and nervous excitement, while symptoms, such as asthenia, throbbing and apprehension, may appear. Early pallor may occur followed after a half an hour or so by flushing, sweating and arterial pulsation. Respiration may become slow and deep and later may increase in rate and diminish in depth. Premature systoles may appear. Various degrees of the reaction may be obtained, but a rise of at least ten beats a minute of the pulse and an increase of at least ten millimetres of systolic pressure are obtained.

In addition to these general symptoms, there is usually a characteristic local reaction. An area of blanching round the point of injection is seen and at the margin of this there is a red areola gradually shading off into the normal skin colour. In about half an hour the centre of the white area becomes bluish-grey or lilac to lavender in colour and in about one and a half to two hours the red areola assumes a lavender colour, persists for about four hours from the time of injection and is the most characteristic part of the test.

Some observers prefer an intradermic injection, also described by Goetsch. For this 0·06 cubic centimetre of a 0·25‰ solution of adrenalin chloride is injected intradermally. In this test the local reaction above described is well seen and is the most important part of the test.

The test is certainly a most valuable one. Goetsch does not claim that all persons who yield a reaction are suffering from hyperthyreoidism, but he says

that the test is an indicator of hypersensitiveness of the sympathetic nervous system. It is probably very valuable in a negative sense. While a reaction does not necessarily imply a state of hyperthyreoidism, failures to react may be most valuable in excluding hyperthyreoidism and in distinguishing it from the neuroses, with which it may easily be confused when present in slight degree.

Treatment.

The medical treatment may be summed up as physical and mental rest in the widest sense, with elimination of all toxic factors, as far as possible, attention to the general health, administration of iodine and quinine hydrobromide and perhaps salicylate of soda and ergotin, attention to symptoms as they arise, many of which can be controlled and alleviated by suitable drugs. I do not propose to discuss the treatment in detail.

The sooner the condition is diagnosed and the earlier and more efficient is the medical treatment, the less frequently will partial thyreoidectomy be required. Septic tonsils must be enucleated, oral sepsis must be treated and intestinal disinfectants, including colonic irrigations or Plombière douches, may be called for.

Diet is most important. It used to be thought that proteins caused increased thyreoid activity and consequently protein was to a great extent eliminated from the diet of patients with Graves's disease. Boothby and Sandiford and others have lately proved that nitrogenous metabolism is not increased in exophthalmic goître and conditions of hyperthyreoidism and therefore cannot be the cause of the increased basal metabolic rate. Consequently it is not necessary to keep the protein down to a minimum. In order to eliminate the excessive heat, large quantities of fluid are necessary. All the patients should be given plenty of nourishment. The calorific requirements of these patients to meet the increased metabolism are very high and at least 4,000 to 5,000 calories and at times more should be supplied.

A cure can be expected only by prolonged treatment. Assuming that the cause is too much thyreoid secretion in the blood, it follows that rational treatment must be directed either to the reduction of the thyreoid activity or the neutralization of the secretion or its effects.

It may be said that efforts in the latter direction by means of serum or the milk of thyreoidectomized goats have proved useless. We are, therefore, compelled to reduce the thyreoid activity. This can be done by means of drugs which will adjust or inhibit the thyreoid secretion or adjust it in some way. Of these the most important are iodine, quinine hydrobromide which is undoubtedly a most useful drug and should always be given when medical therapy is instituted, ergotin and perhaps salicylate of soda and arsenic; or by cutting off the supply as in surgical measures, X ray and radium treatment.

Medical remedies are certainly not always satisfactory in the present state of our knowledge. Medical therapy, however, should always be carried out especially if the patient is seen at a comparatively early stage. The patient should be given the benefit of proper medical therapy with rest in bed unless this is contraindicated. When medical treatment fails or causes no improvement in the condition, we must rely on either X ray or radium therapy or surgical removal of a portion of the gland or some other operative measure.

THE PRESENT DAY POSITION OF IODINE AS A MEANS OF THERAPY IN HYPERTHYREOIDIC CONDITIONS AND GRAVES'S DISEASE.

Laboratory observations point to a perversion of the normal secretory processes of the thyreoid gland in hyperthyreoidic conditions. It has been shown by estimating the total iodine in the thyreoid in Graves's disease that there is present only one-twentieth to one-fiftieth of the normal amount of iodine proportionately to its weight. This goes to show that the gland is not attaching iodine to the normal extent. It is not possible, however, to look upon the causation simply as an iodine deficiency. It is true that Marine has shown that when the iodine store of the normal thyreoid falls below a certain minimum (0·1%) and this continues, a definite cellular proliferation and hyperplasia supervene. But this is not Graves's disease and the normal can be restored by iodine feeding. Although iodine has been used in treatment of goître for centuries, it was found at times to cause symptoms of thyreoid intoxication or to increase those already present. Stimulated by its efficiency in simple goître and by the work of Marine and Lenhart, who showed that the iodine content of the gland was reduced in hyperplasia, many workers have tried it in exophthalmic goître and the good results obtained by Plummer and Boothby, of the Mayo Clinic, have stimulated its use all over the world. The consensus of opinion at present is that it can induce in primary Graves's disease a striking remission in the severity of the intoxication, but that it is in no sense a cure. Usually cessation of the iodine administration causes a relapse and a resumption of iodine therapy seems to have less effect after such a relapse than it had at first.

Prolonged overdosage can do harm. A daily dose of fifteen drops of Lugol's solution or of a 10% solution of iodine in 95% alcohol will give a maximum effect in a week to ten days, but for prolonged administration it is better to reduce the dose to five drops a day or else to give iodine in the form of small doses of potassium iodide. As a result of iodine the basal metabolic rate and the pulse rate fall in as striking a manner as after subtotal thyreoidectomy, but the change is not so persistent. Probably with long continued administration the disease runs its course at a lower level of toxicity and if it is stopped, patients usually do not feel quite so well.

There is no doubt that by the use of iodine patients can be brought to a much more satisfactory condition for surgical treatment than would otherwise be possible. Indiscriminate administration of iodine is still as dangerous as when Kocher issued

his warning and it is certain that the reintroduction of this method of treatment is at present frequently resulting in harm.

However, if carefully handled, it is certainly a most valuable drug. At first sight it seems extraordinary that the same drug should be used in both hypothyreoidism and hyperthyreoidism. It is probable that the enlargement of the gland in the former condition associated with certain forms of simple goître is often symptomatic of iodine starvation, while in the latter condition the secretion, though increased in amount, is not adequately saturated with iodine. Thyroxin should contain 65% of iodine distributed as four atoms round the two benzine rings it contains. Iodine seems necessary to the resting gland; if this is lacking, the gland is in a condition of unrest and the secretion abnormal. If iodine is supplied, the symptoms improve until enough has been given to saturate the thyroxin with its four atoms, but if the dose is then maintained at the same level, after saturation has been reached, there will be too much iodine and the symptoms again become aggravated. This suggests that excess of iodine may stimulate the further production of thyroxin. We know that there is a definite iodine metabolism in the body, but we have no means of estimating the iodine contents in the body as we can the blood-sugar content. The dosage is purely a matter of guesswork and may be right or wrong. If we were able to estimate in definite quantities the amount of iodine in the thyreoid gland deficient or in excess, our therapy would be very simple and exact and our results accordingly very successful. There is no doubt that large doses of iodine given in the form of Lugol's solution (from 1·2 to 2·4 mils of the solution, that is, twenty to forty minims *per diem*) for three to five days before operation, the dose given depending on the severity of the symptoms, has profoundly altered the immediate prognosis of the operation. Even though it may be temporary, there is a definite regression of all symptoms, particularly the tachycardia, the restlessness and the excitability. The remission of symptoms known as the iodine remission is usually striking and occurs in 80% to 90% of patients. The patient begins to feel well and approaches a normal state of composure of mind and body. The iodine is the cause of this remission. It does not cure, as recurrence of hyperthyreoidism gradually sets in, may be in exaggerated form, during the course of too prolonged iodine administration, while the hyperthyreoidism may return even more suddenly if iodine administration ceases; suitable small doses may, however, be given for many months or even some years with great benefit.

It has been stated that in extremely toxic cases the use of Lugol's solution in Graves's disease approaches in value the use of "Insulin" in diabetic coma. In very severe cases when operation is temporarily contraindicated, iodine administration has given almost miraculous results.

Regarding the use of iodine in Graves's disease, it may be said that much harm may result from its injudicious administration, that it is not only invaluable as a means of preparing the patient for operative treatment, but under certain conditions may prove very beneficial treatment for the disease itself, that its administration may be continued for months with progressive benefit, that no other drug ever used has shown the same remarkable therapeutic action, that the initial dose of iodine given to correct the defect is required only for a few days or weeks and the dose should be reduced as soon as improvement has set in, that close observation of the pulse rate, pulse pressure and weight of the patient is required during either a short or a prolonged course of iodine treatment, that increasing hardness of the thyreoid is an indication for a smaller dose, that the results of iodine treatment justify the view that Graves's disease is a primary deficiency disease, even if it does not furnish evidence to prove it.

In Graves's disease complicated by jaundice, iodine and glucose are the best form of treatment. The method of administration of iodine recommended by Plummer is to give 0·3 mil of Lugol's solution by mouth and in severer cases up to 0·6 mil thrice daily. In less severe cases it may be given twice or even only once daily. It should be given well diluted in water and followed by half a glass of water. Its ideal use seems to be as a preparatory measure for operation and it may then be given even for a week or ten days and for patients with less toxic conditions for three to five days before operation is undertaken. This seems to avoid the dangerous post-operative crisis which used to be the bugbear of every surgeon and will tide the patient over a most dangerous period until the good effects result from the operation.

Following operation iodine may still be required and when it is unwise to give it orally, for example, when there is severe vomiting after operation or in association with a crisis, it may be given *per rectum* as an enema well diluted. In such emergency 0·6 to 1·8 mils of Lugol's solution may be administered.

Perhaps next to its value as a preoperative preparatory measure, is the benefit of iodine in the many crises that are characteristic of Graves's disease. For these it may be given three or even four times daily in severe cases for a few days, but the dose must be gradually reduced to once a day as soon as improvement takes place.

Finally its value as a therapeutic and palliative measure for prolonged administration must be considered. Apart from crises it may be given twice or three times daily, if indicated in severe cases, for a few days. If we wish to continue its use, perhaps the best way is to give periodic courses lasting from seven to ten days or even longer if the patient is improving and during the interval to give small doses of potassium iodide. In this way the course of Lugol's solution may be repeated every month or at longer or shorter intervals according to the severity and toxicity of the condition, the reaction to treatment and the progress made. Thus one will get over the difficulty of the common

clinical experience that as soon as Lugol's solution is discontinued, the symptoms are liable to reappear, inasmuch as the iodine is not being completely withdrawn, but is continued in the form of the iodide.

In considering the therapy of this disease and the value of iodine, I must emphasize the results obtained by Cowell and Melanby in studying the effects of iodine on hyperthyreoidism in man, the iodine being given in the form of potassium iodide. In every case of hyperthyreoidism observed in their series the giving of small doses of iodide resulted in a distinct clinical improvement. The improvement was obvious at the end of a week and the slowing of the pulse rate, the lowering of the basal metabolic rate and the lessening of the general nervous excitability attained a maximum between the tenth and twentieth days of the treatment. From this time onwards there was considerable variation in the response of different patients and this response may show itself in one of three ways.

(i) They may remain for several weeks in this greatly improved condition with a low basal metabolic rate and a slow resting pulse rate and then develope a very slight and gradual return of the symptoms, although they are much improved as long as they continue the iodine treatment.

(ii) There may be a sudden or a rather sudden return of the symptoms soon after their maximum decline, but the patients continue to put on weight and regain strength in spite of an increased metabolism and tachycardia. These two classes comprise the main bulk of patients.

(iii) Occasionally there may be a more violent exacerbation in which the symptoms return within the course of a week or two to their original degree of severity. It is not possible to predict with certainty what course is likely to be followed by any particular case. Usually, however, those patients with large hard glands are more likely to develope severe reaction symptoms than those with smaller soft ones.

It was most striking in their series of cases that the amount of iodine given does not appear within certain limits to control the rate of improvement noted in the early stages of treatment. Administration of 0·45 gramme of potassium iodide daily was followed by much the same improvement observed as when only six centigrammes daily were given in two divided doses. But it was further noticed that when very small doses were given, the return of any symptoms tended to be longer delayed and were less severe than when large doses were given. It has not been determined what is the minimum quantity of iodide that will exert a demonstrable effect, but it is less than three centigrammes a day. When a return of the symptoms occurred, while the patient was receiving a small dose of potassium iodide, it was found that if the dose were increased under these conditions, a still further exaggeration of the symptoms occurred.

Withdrawal of the iodide was followed almost invariably by an increase in the severity of the symptoms, while resumption was invariably followed by a rapid return to the state that existed before the withdrawal.

It is not possible to say what is the effect of iodides on the structure of the thyreoid; not uncommonly the gland becomes larger and firmer during the first few weeks of treatment, pulsation usually diminishes and may disappear and in some cases there is a slow and steady diminution in the size of the goître. During the more severe exacerbations the glands may increase in size and show signs of increased vascularity, but this change is not constant.

From the practical point of view the giving of small amounts of iodide to patients suffering from hyperthyreoidism is a valuable adjunct to other medical treatment and it is possible that doses of the order of six milligrammes daily or even much less of potassium iodide will prove to be the most suitable for the majority of patients.

Iodine Hyperthyreoidism.

In our enthusiasm for the efficacy of iodine in the treatment of exophthalmic goître, we must not forget that injudicious use will produce a symptom-complex known as iodine hyperthyreoidism. It must be recognized that while beneficial effects may attend the use of iodine in the treatment of goître, grave harm may be inflicted by it. Kocher was the first to call attention to the possible dangers of iodine therapy and later on it became more fully recognized that the administration of iodine might produce in certain goîtrous subjects a syndrome which resembled Basedow's disease or exophthalmic goître, but which was quite a separate clinical entity. Many kinds and preparations of iodine may cause iodine hyperthyreoidism. The various so-called goîre cures, most if not all of which are iodine preparations, the many liquid forms of the syrup and tincture, ferrous iodide preparations and many more may cause it. Some persons apparently have a relative immunity, while in others toxic symptoms may result from even small doses of a few weeks' administration. It is interesting to note that the number of cases of iodine hyperthyreoidism has greatly increased in recent years as a result of the popular demand for iodine in the treatment of goître. This is all the more important as many of these patients can be brought through their serious condition only with the greatest difficulty, while occasionally the result is fatal.

This naturally brings up the question whether it is practicable or safe to distribute iodine promiscuously either in water or food or whether it should be administered only in exact amounts under a physician's orders. The variable and often very small amount of iodine necessary to produce toxic symptoms in persons with adenomatous goîtres makes one consider whether the wholesale distribution of iodine by way of drinking water or table salt is advisable. Although these are undoubtedly steps in the right direction as a means of preventing goître, especially in endemic areas, the effect of this wholesale use on the general population must be

taken into consideration. Some say that the amount each person receives is so infinitesimal that it cannot do any harm and others contend that the amount of good done would greatly outweigh any harm resulting, but if there is any danger at all, great hesitation must be shown before any such wholesale distribution is authorized. Perhaps if any of these methods are practicable, distribution in the form of salt is one of the best, but the dose must need be very accurate and variable. Some children especially use a great deal of salt, while others use very little; then again some may take a great deal of salt one day and then go several days without any. Consequently it can easily happen that a child who needs much iodine, will get relatively a very small amount, while a child who needs none or very little, may get a good deal.

Probably this difficulty could be surmounted if the amount were restricted to a minimum dose, even though in many cases it was an insufficient one.

The distribution through drinking water is even more difficult and it has never been considered practicable because of its great waste. The water may be iodized in a strength that will make each 22·5 litres of water contain one milligramme of sodium iodide. Whether or not such small doses of iodine are sufficient to initiate symptoms of hyperthyreoidism in a case a non-toxic adenoma is still a vexed question.

Effect of Iodine in Various Types of Goitres.

Marine and Kimball tell us that iodine administered to children and persons under twenty-one years of age for the prevention or treatment of colloid goître is practically harmless if the drug is given in small doses. Iodine should, however, be administered with great care to children with adenomatous goîtres, while it should never be given to adults with this condition. In people over twenty-one years of age with adenomatous goîtres even minute doses of iodine are sufficient to initiate symptoms of hyperthyreoidism; it is contra-indicated.

On the whole, iodine hyperthyreoidism is rare in persons under thirty and it developes only in the presence of an adenomatous goître. Probably iodine is of no avail in the treatment of goître except of the exophthalmic type (Graves's disease) after the age of twenty-one and with increasing age the risk increases.

Clinical Symptoms Characteristic of Iodine Hyperthyreoidism.

The clinical syndrome may be clearly distinguished from that seen in toxic adenoma or exophthalmic goître. The syndrome of iodine hyperthyreoidism is not typical of either toxic adenoma or exophthalmic goître and yet presents many symptoms common to both and consequently is a condition easily differentiated as a rule. Thrills, bruits and exophthalmos do not occur. It rarely is seen before the age of thirty, though occasionally it may be seen in young children. It is also rare in elderly people. The same tremor, loss of weight and strength, tachycardia, restlessness and insomnia occur as are seen in toxic adenoma and Graves's disease. The onset of symptoms and the loss of weight are, however, rather more rapid and severe than in toxic adenoma and in these respects it resembles Graves's disease more closely. The tachycardia is just as severe and persistent as in exophthalmic goître and there is little or no response to digitalis. Apparently the iodine exerts a toxic antagonistic effect on the myocardium that renders it immune to the action of digitalis. The basal metabolic rate more closely resembles that of toxic adenomata, the average being less high, being between + 25% and + 35%, while an average figure in a well-developed Graves's disease is in the region of + 40% to + 50% and even higher. The pulse pressure in this condition is usually elevated, but the blood pressure findings closely resemble those seen in toxic adenoma.

It goes without saying that the further administration of iodine will still further aggravate the symptoms of iodine hyperthyreoidism, but in a case of Graves's disease great improvement will take place with iodine even if it is only temporary, so that although this point may be used as a means of diagnosis in very doubtful cases between these two conditions, naturally it is a means that should be used only with the very greatest care and caution.

Treatment of Iodine Hyperthyreoidism.

If iodine hyperthyreoidism is diagnosed early, it is possible to cut short the toxic symptoms by withdrawing the iodine and by medical means. If the symptoms are not becoming progressively worse, the patient should be treated energetically for ordinary hyperthyreoidism.

When the condition does not yield quickly to medical measures, thyreoidectomy must be performed, but in all cases of this nature operative measures are always attended with very great risk.

Pathology.

The pathological picture is not characteristic. The gland has the appearance of an adenomatous goître containing degenerated cystic, fibrous and calcareous encapsulated nodules. Colloid may be seen in large amounts. It never has the typical beefy appearance of the exophthalmic type, with its alveoli composed of epithelial hyperplasia without colloid.

Probably this type of hyperthyreoidism can best be accounted for on a physiological basis, in that there is a disturbance in the iodine metabolism. The views on this point are so numerous that no purpose will be gained by a discussion of them and until the pathologists are able to explain to us more specially the various pictures seen in simple and toxic adenomata and exophthalmic goître as well as in iodine hyperthyreoidism, the true explanation of these conditions will be obscure.

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EARLY TREATMENT OF INFECTIONS OF THE HAND.

By JOHN HOETS, M.B., Ch.M. (Sydney), F.C.S.A.,

Honorary Assistant Orthopædic Surgeon, Lewisham Hospital; Honorary Assistant, Department of Orthopædics and Special Therapeutics, Sydney Hospital.

AT the outset I will admit that my results in repair of hands damaged by sepsis will not bear comparison with those quoted by Sterling Bunnell[1] in the masterly article on this subject in the January issue of the *Journal of Bone and Joint Surgery*. My experience is that sepsis in severe grade leaves a hand permanently crippled to a greater or less extent and that treatment must extend over months and even years to get even moderately good functional repair. The article quoted above and a film prepared by another master, Kanavel,[2] which I have recently enjoyed seeing screened, have prompted this communication.

The first mentioned deals with repair of nerve and tendon following destruction by sepsis, the second deals fully with and demonstrates beautifully the paths of infection and the correct incisions for draining the various spaces in the hand when they have become infected and filled with pus.

My object is to urge even earlier treatment aimed at limiting the spread of infection and if possible even at preventing pus formation which I believe to be frequently possible. Even if pus has formed and incisions made, we know only too well that the spread is often not checked and a common experience is for more and more incisions to be necessary.

As to the best placing for such incisions I would again refer to Kanavel's film and suggest that every surgeon should do his best to see this picture. It is the best exposition of hand sepsis and its surgical treatment I have seen.

Diathermy applied early and frequently to a local infection will often keep it localized and, if applied early enough and often enough, may prevent pus formation. Pus having formed and been evacuated, this method of treatment will help to stop further spread and hasten recovery in a very pronounced degree.

Technique of Application of Diathermy to Sepsis in the Hand.

One electrode is in the form of a metal cuff applied above the wrist at a convenient place in the forearm, provided it is well above the uppermost limits of infection. The tips of the fingers and thumb dip into a dish of hypertonic saline solution which constitutes the other electrode, the cord to the machine being connected to a piece of lead sunk in the saline solution at as great a distance from the nearest digit as the size of the dish will allow. The current is then passed and increased gradually until there is a sensation of distinct warmth in the fingers or wrist, usually the meter reading about 400 milliampères. A greater current is not necessary or advisable at this stage, as will be seen later. Now the beauty of this technique will be exemplified, as the current passing through the infected digit may be varied at will by simply lifting one or more of the unaffected fingers out of the saline solution. That is, if the thumb be in trouble, the little finger is first raised, then the ring, then the middle, then the index finger, thus throwing all the current towards the radial side of the hand. When the limit of tolerance is reached, the raised finger or fingers may be reinserted into the saline solution and so the current is eased off through the affected part.

Thus the patient can without alteration to the setting of the machine keep the part being treated at the greatest degree of heat he can tolerate for the whole period of treatment.

Frequency and Length of Treatments.

The ideal would be to have the part under treatment continuously until infection was controlled. This is not practicable. The best that can usually be achieved is several, two, three or four periods of forty to sixty minutes each per day. In the interval the part should be kept as warm as possible by means of compresses *et cetera* and, if already incised, with absorbent dressings. The effect of diathermy on the discharge is interesting. As soon as the hyperæmia is established, the discharge begins to pour away with much greater freedom and becomes increasingly more fluid until it is after a greater or less number of applications serous; when this stage is reached, the infection may be looked upon as beaten.

Radiant light and heat may be used with advantage as an adjunct in the treatment, but the above mentioned is, I believe, of the utmost value in control of sepsis.

Illustrative Cases.

The following are illustrative cases:

CASE I.—Dr. A., practising in the country, had the index finger of his left hand infected three months previously. The finger had been opened and the usual remedies applied, that is, fomentation *et cetera*. The infection did not spread further, but became indolent. A pocket of pus

would form, discharge through the old incision, remain apparently well for a day or two and repeat. This had gone on for three months, during which time no surgical or obstetrical work could be undertaken. He came to Sydney and consulted a surgeon who contemplated further opening up, but was loath to do so on account of possible mutilation and loss of function. In consultation I suggested diathermy with the idea of producing active hyperæmia. I had not then seen what diathermy was capable of in the face of sepsis. In two weeks from the first treatment the finger was perfectly well and did not break down afterwards.

CASE II.—Dr. B., in doing tonsillectomy, was bitten rather severely on the base of the index finger of the left hand about ten days previously. I noticed the bandaged finger and inquired of the injury. We were playing tennis. On removal of the bandage we were alarmed at the sight. A dirty purplish ulcer about the size of a threepenny bit was surrounded by a dusky areola. Diathermy and ultra-violet light began the same day and in a week the finger felt normal and the surface of the ulcer, now practically healed, and the surroundings were a healthy pink colour. Improvement began immediately on institution of treatment.

CASE III.—DR. C. had some old infected scar tissue on one foot. This infection occasionally would flare into activity and had on each occasion caused abstinence from work for over two weeks. On the last occasion as soon as signs of activity were noticed, on my advice he retired to bed with a portable diathermy machine beside him. Treatments were given three times a day for forty minutes each and he was back at work on the fourth day.

CASE IV.—Miss D., a masseuse, noticed some cracks about the nail of the thumb of the right hand. These were sore and a few days later the distal joint felt stiff with some swelling and pain extending from the base of the nail up the forearm. There was definite tenderness on both the flexor and extensor aspect of the thumb to the wrist. Under local "Kelene" anæsthesia several incisions were made about the terminal phalanx and diathermy started. Treatment was given several times daily. Incisions were made on three successive days, all about the terminal phalanx and pus was evacuated in large quantities. The tenderness gradually subsided and at the end of two weeks from the first incision the digit was practically well with free mobility of the joint and no extension proximal to the terminal phalanx.

References.

(1) Sterling Bunnell: "Repair of Nerves and Tendons of the Hand," *Bone and Joint Surgery*, January, 1928.

(2) Film, Kodak: "The Diagnosis and Treatment of Infections of the Hand," by Allen B. Kanavel. Film produced by Eastman Kodak Company, in conjunction with the Committee on Medical Motion Pictures of the American College of Surgeons.

Reports of Cases.

DUODENAL ILEUS.

By M. P. SUSMAN, M.B., Ch.M. (Sydney), F.R.C.S. (England),

Honorary Assistant Surgeon, Royal South Sydney Hospital.

Clinical Findings.

T.W., aged twenty-three years, was admitted to hospital with a fracture of the left tibia and fibula. While under treatment for this, he commenced vomiting. His relatives stated that he had been subject to many such attacks since childhood and his illness at first was not regarded seriously. Soon, however, his condition deteriorated, absolute constipation ensued and the vomitus became dirty and offensive.

He looked cachetic, with sunken eyes and sallow complexion. His tongue was dry and furred and his breath foul. He had no pain. Examination of the abdomen revealed no abnormality except for the observation that it was retracted and dull to percussion. Enemata were returned clear without force or flatus.

The stomach was washed out before operation.

Operation.

I opened the abdomen through a right paramedian incision. Many coils of small gut were adherent to one another and to the anterior abdominal wall. All were collapsed; the large intestine and the stomach were empty. At this stage the patient's condition suddenly became worse and the abdomen was closed without further investigation.

Autopsy.

The stomach and the duodenum were very distended; the rest of the alimentary tract was empty and collapsed. The obstruction seemed definitely to be due to constriction by the superior mesenteric vessels.

Comment.

The previous attacks of vomiting were doubtless due to less severe and less persistent obstruction. It is noteworthy that the fatal attack occurred while the patient was confined to bed. Acute obstruction of the duodenum by the superior mesenteric vessels was described first by Rokitansky in 1842, but chronic obstruction from this cause was not recognized till 1908 (Staveley).

This case is apparently one of chronic duodenal ileus, ending with acute obstruction.

Symptomatology.

Chronic duodenal ileus is more common in women than in men. The patient usually complains of attacks of flatulent dyspepsia with epigastric pain or distress a half to two hours after meals, anorexia, nausea and constipation. Frequently there is a history of bilious attacks for years, that is, headaches, nausea and bilious vomiting; as in my patient, there may be no complaint of abdominal pain. Sometimes there is only chronic epigastric discomfort and distension after meals. The patient is often of neurotic temperament, and may receive little sympathy from friends or doctor.

Examination may reveal no abnormality.

The following signs have been noted by different observers:

1. A large splashing stomach.
2. A dilated duodenum, with or without the splashing stomach.
3. Local tenderness just to the right of the navel.
4. The "pressure paradox," that is, relief from pain and tympanities by pressure upwards and backwards at a point just below the navel; this pressure causes the gas in the duodenum to pass into the jejunum.
5. In the case here reported the combination of flat abdomen and dull percussion note over the intestines with symptoms of high intestinal obstruction was very striking, although its significance was not realized until the collapsed gut was seen at operation and the obstructed duodenum at autopsy.
6. Radiography has revealed a low, hypotonic or dilated stomach, with delayed emptying; a greatly enlarged duodenal cap and occasionally duodenal antiperistalsis.
7. Spontaneous relief when the patient assumes the prone or genu-pectoral position.

Differential Diagnosis.

A history of bilious attacks and headaches with little or no abdominal distress may lead to the diagnosis of migraine or, if the patient is a child, of acidosis. When the patient is a neurasthenic female, simple visceroptosis may be thought sufficient to account for her symptoms. Gall

bladder disease and peptic ulcer (especially when complicated by pyloric stenosis) must be considered when there are definite post-prandial abdominal symptoms. Both of these conditions have been known to coexist with duodenal ileus.

Pathology.

The following conditions have been found by different observers:

1. Compression by the superior mesenteric vessels with proptosis of the mesentery and its gut.
2. Compression by the right colic artery with a proptosed and mobile proximal colon.
3. Pressure due to thickening and infiltration of the root of the mesentery, for example, chronic inflammatory, tuberculous or malignant.
4. Gastroptosis. The dropping of the distended stomach drags on the duodenum and causes kinking at the duodeno-jejunal flexure.

Treatment.

Medical treatment and an abdominal support are sufficient in some cases.

Surgical treatment varies with the underlying pathological cause:

1. Duodeno-jejunostomy is indicated when the obstruction is due to pressure by the superior mesenteric vessels or by a thickened mesentery.
2. Posterior gastro-enterostomy has been successful when gastroptosis was the cause.
3. Coloplexy is done when a prolapsed ascending colon is responsible.

Bibliography.

D. P. D. Wilkie: "Duodenal Ileus," *The British Journal of Surgery*, October, 1921, page 204; *The British Medical Journal*, December 23, 1922, page 1219.

J. E. Adams: "Duodenal Ileus," *The British Journal of Surgery*, July, 1926, page 67.

Reviews.

STOMATOLOGY.

"DISEASES OF THE MOUTH," by Sterling V. Mead, D.D.S., is a volume of some five hundred and seventy-eight pages with two hundred and seventy-four illustrations and twenty-nine full page colour plates.[1]

The author presents it as a textbook for dental and medical students. It certainly appears to go very thoroughly into the dental diseases.

The first sixteen chapters are taken up by descriptions of diseases of the teeth, diagnosis, prognosis and treatment. On account of the very detailed description this part of the book would naturally appeal more to the dentist than to the medical practitioner.

The remainder of the book does not appear to be very helpful. We feel that an effort has been made to condense under many headings all the conditions that may affect the mouth in the remotest degree. Accordingly there is much repetition of symptoms and no particular section is of great practical value.

The specific infectious diseases are dealt with in twenty-three pages, including many illustrations. Other chapters include those on diseases of the blood; diseases of the nerves; diseases of the tongue; of the throat and of the salivary glands.

In the description of maxillary sinus diseases the part played by septic teeth in the causation of infection of this sinus is emphasized, but the statement that "in 75% of sinus involvement there is some infection in the mouth which may be a contributing factor, if not the entire cause of the disturbance" appears to be much exaggerated.

Ascending osteitis spreading to the frontal and ethmoidal sinuses occurring as a complication of an infected maxillary antrum is hardly of such frequent occurrence as the author indicates.

The part describing cysts of dental origin is more helpful, but in proportion to the size of the book we think that more space could have been devoted to this section.

The author conveys the general impression that he does not find X ray films very reliable as an aid to diagnosis, though the book is profusely illustrated with X ray pictures.

Seventy-six different forms of stomatitis are given—from that due to beri beri to that due to menstruation.

The book is well presented and the illustrations are exceptionally good, but it is impossible to recommend this volume to the general medical practitioner as a textbook.

[1] "Diseases of the Mouth," by Sterling V. Mead, D.D.S.; 1927. St. Louis: The C. V. Mosby Company; Melbourne: Stirling and Company. Royal 8vo., pp. 578, with illustrations. Price: $10.00 net.

A BOOK ON EPILEPSY.

THE student of epilepsy will find material for much consideration in "Epilepsy," by Dr. L. J. J. Muskens, of Amsterdam.[1] The author presents to the reader the result of a lifelong study. The book is divided into three parts dealing respectively with the physiological problems involved in epilepsy, anatomo-physiological research and the clinical part or personal experience. The author is a disciple of the British and American school of neurology which is a fact much appreciated by the majority of neurologists. The author's idea of epilepsy is that it is a method of discharging an organism from the influence of a toxic substance. He lays great stress upon the importance of the myoclonic shock as a prodrome to the epileptic fit. The terms myoclonic start, myoclonic shock, myoclonic reflexes and myoclonic epileptic fit are fully explained early in the book in conjunction with the description of the experimental work done upon animals, mostly cats. Dr. Muskens is of the opinion that the centre of the myoclonic reflex is also the centre for the reflex after-discharge or epileptic fit. The quantity of experimental work recorded is enormous, but there is a tendency in it as well as in other parts of the book to needless repetition. There is considerable space devoted to the results of experimental sectioning of nerves and the creation of lesions in various parts of the central nervous system. To some extent the psychical aspect of the question is neglected. In fact the statement appears to the effect that essential epilepsy is not psychological, apparently to show that this author has no sympathy with the school which considers the epileptic fit a way of side-tracking the reality of life. The clinical section is far and away the best part of the work and should be of great value as a guide to investigation and treatment. Here again there is missing the information on the psychical complications that a work of this magnitude should not lack. The references to the opinions of other workers are very extensive. One section deals with the importance of the examination of drivers of motor omnibuses and trains. This is in order to anticipate epileptic fits in a dangerous occupation by detecting the presence of past myoclonic shocks which the author regards as important danger signals in this disease. Several classifications of epilepsy are given with a reminder that they are all difficult.

The section dealing with operative measures in the different types of convulsions should make all readers ask themselves if they have not been too conservative in regard to advising operative interference in the past. The author's experience in this branch of the work has been singularly happy and the reader is impressed by the fact that the author seems particularly sure of himself in these conditions. The last chapter outlines means for the prevention of epilepsy and for the care of the epileptics in a country. The appendix includes a list of the proprietary remedies for epilepsy, most of them being carelessly weighed, which in itself means danger for the patients. This book appears to be the most comprehensive of the present day works upon the subject of epilepsy and on that account can be strongly recommended to those interested in the subject.

[1] "Epilepsy, Comparative Pathogenesis, Symptoms, Treatment," by L. J. J. Muskens, M.D.; Foreword by Sir Charles S. Sherrington, O.M., G.B.E., M.D., D.Sc. (Cambridge), F.R.C.P., F.R.S.; 1928. London: Baillière, Tindall and Cox. Royal 8vo., pp. 449, with illustrations. Price: 27s. 6d. net.

The Medical Journal of Australia

SATURDAY, MAY 26, 1928.

A Matter of Tariff.

THE Commonwealth Tariff Board is holding public inquiries concerning certain duties imposed on goods imported into Australia and the medical profession in common with other sections of the public is being invited to tender evidence in support of or in opposition to the requests that have been made for modifications of the existing tariff. The subjects of immediate inquiry are restricted, but the opportunity will be seized by representatives of the Branches of the British Medical Association in the several States to urge on the Board the views oft expressed that duties on instruments, apparatus and drugs used in the treatment of disease should be remitted in the public interest.

The Customs Department of the Commonwealth of Australia exists for the purpose of providing revenue. It is claimed that preferential tariffs enable the Australian manufacturer to compete successfully with his foreign competitors and thus act as stimulating agents in the development of home industry. It is outside the province of a medical journal to discuss a matter of general policy, in this connexion the relative wisdom of free trade or protection. The medical profession as a section of the community is concerned solely with the treatment of disease and injury and its views on any matter involving the cost of the maintenance of health must be taken into consideration. Whether the individual members of the profession are disciples of Cobden or followers of protective policy, as a body they are opposed to the introduction of commercial argument into questions of life and death. This aspect of the matter may be dismissed with the statement that it is not worth while for a Minister for Customs to resist the demand of the medical profession, in view of the relatively small amount of money involved in duty imposed on goods destined to be used in the preservation of life and health.

The contention of the medical profession is that no government is justified in imposing charges that increase the cost of treatment of disease or injury. It might be just if these charges were borne by the well-to-do members of the community, but in actual life it is the hospital and the sick poor who have to pay. If an instrument, a piece of apparatus or a drug is needed for the most effective treatment of disease, it is without question in the interests of the nation that that instrument, that piece of apparatus or that drug should be obtainable for every sick person at the lowest cost possible. Disease inevitably means the heaviest burden that the community has to carry. The prosperity of a nation is directly proportionate to the mental and physical vigour and health of its individual members. In modern times treatment has become inordinately expensive, owing to the complicated and elaborate weapons employed. Radium cannot be prepared except at a very high cost; X ray apparatus has to be constructed with meticulous care and at considerable expense; other instruments of precision essential for the diagnosis and treatment of diseases cannot be produced without the expenditure of research and exquisite skill in manufacture. The chemist synthesizes new drugs after years of painstaking investigation and experiment and his materials are rarely cheap. Moreover, we claim that the government, the medical profession as a whole and the schools of medicine cannot be accepted as the sole judges of the value of any one method of treatment. Provided that the remedy is an honest one, it must be left to the decision of the individual practitioner whether it or some other means should be employed in the treatment of a particular patient. It would therefore be wrong to make a selection or to set up a list of orthodox instruments, apparatus and drugs to receive official recognition.

It may be argued that if an X ray apparatus is manufactured in Great Britain, another in Australia, another in the United States of America and another on the Continent of Europe, customs duty might reasonably be levied on the last two in

order to protect the commercial interests of the makers of the first two. This argument is invalid, for it is impossible without years of experience and experiment to determine whether the first, the second, the third or the fourth apparatus yields the best results. Probably all four are the best under special circumstances that vary with individual users, individual patients and individual diseases. No argument can be adduced in favour of a duty on X ray apparatus, X ray tubes, surgical instruments and therapeutic drugs no matter where these things are produced. A government that is prepared to collect money at the expense of the citizens, must answer the charge of sacrificing life for a temporary financial gain. But even if a government were so careless of the welfare of its citizens, it would need to consider the economic aspect of the matter. To render the treatment of disease difficult and expensive means that the health of a considerable number of impecunious persons would be sacrificed and eventually the mass of unemployable men and women would be increased. Unemployment has always proved a very costly problem to a nation and vast sums of money are expended in the endeavour to reduce it.

The subject of inquiry at present before the Commonwealth Tariff Board can be solved without difficulty. Instead of protecting the interests of a few manufacturers of X ray transformer apparatus and of surgical instruments and appliances in the vain hope that the medical profession will be coerced into the exclusive use of these means of treatment, whether or not they are superior to imported instruments, appliances or apparatus, all should be admitted into the Commonwealth free of duty for the benefit of those Australians who unfortunately are in need of them. These things are expensive enough without adding a preferential tariff of 27½%, an intermediate tariff of 35% and a general tariff of 40% of their original value. This is the duty imposed at present on X ray transformers other than those designed exclusively for deep X ray therapy. We trust that the Department will exercise reason and not insist on the application of a principle when it affects the health of the community.

Current Comment.

CANCER OF THE RECTUM.

CANCER of the rectum is in many respects different from cancer in other parts of the body. It makes its appearance insidiously and progresses slowly; it is so situated that by the time it is discovered it has frequently progressed to such a distance into the surrounding tissues that operation is a very hazardous undertaking; it should be diagnosed without difficulty—a digital examination will reveal its presence and yet at the present day it is overlooked by medical practitioners. In these circumstances consideration may well be given to some of the more important aspects of this disease.

One of the most useful methods of studying a subject is to review the literature and collate the accumulated experience of different workers. The Departmental Committee on Cancer of the Ministry of Health of Great Britain has recently completed an inquiry into cancer of the rectum.[1] The report is based on the records of 6,000 cases of rectal cancer in which medical operation was undertaken. The literature of ten different countries was examined by F. J. Darbyshire and in addition the Departmental Committee had the assistance of the Surgical Statistics Subcommittee and of Lane-Claypon and Greenwood. The report is a document of some seventy pages and consists largely of statistics. It will be impossible to consider every aspect of the report; reference will, therefore, be made only to those points which appear to be of the most practical importance.

It is obvious that in any discussion on malignant disease of the rectum it is necessary to specify the limits of the area under consideration. Many authors have pointed out that it is impossible to consider rectal tumours apart from those of the pelvic colon. In this report they have been considered together. The tumours have been divided into three groups: low, middle and high. Those described as "low" are situated within 3·75 centimetres (one and a half inches) of the anus. The "middle" group includes tumours from the 3·75 centimetre level to a distance 11·25 centimetres (four and a half inches) from the anal margin, in other words tumours within reach of the examining finger. The tumours in the "high" group were situated more than 11·25 centimetres from the anus and included those of the recto-sigmoidal junction.

The chief types of operation undertaken were the perineal, the sacral and a combined operation, that is, an abdominal operation combined with a perineal or a sacral one. Operations through the abdomen only or excision by way of anus or vagina were undertaken so seldom that they need not be considered in this place. It is interesting to compare the frequency with which the different types of operation were performed in the ten different countries. The four countries with the largest

[1] Reports on Public Health and Medical Subjects. Number 46. "Report on Cancer of the Rectum: An Analysis of the Literature with Special Reference to the Results of Operation." Ministry of Health, London, 1927.

number of operations to their credit are Germany, Austria, the United States of America and England. In Germany 1,673 radical operations were performed; 32·4% of these were of the perineal type, 51·6% of the sacral type and 7·7% of the combined type. The number of operations in Austria was 1,289 and the percentages of the three types of operation were respectively 1·6, 92·9 and 4·2. In the United States of America the total was 1,255 and the percentages for the three types of operation were 10·9, 6·2 and 10·1. In England the total was 573 and the percentages were 60, 16·9, 8·9. It is but natural that the sacral operation should be more popular in Austria and Germany where it was introduced by Kraske in 1885. An important part about these records, however, lies in the fact that in a great many instances no record was made of the type of operation performed. In the United States of America the operation was not described in 69·5% of cases. In England 13·1% of operations were not described; in Germany the percentage was 5·2 and in Austria only 0·9. Right through this report the same thing crops up repeatedly and is the first point on which emphasis should be laid. Surgeons undoubtedly operate with the immediate welfare of the patient as a primary consideration. They owe something at the same time to the common fund of knowledge and to the art and practice of surgery. By keeping accurate records they can do something in both these directions.

The next question to be considered is that of operability. This will obviously depend on the experience, skill and judgement of the surgeon and on the stage of the disease at which he sees the patient. While many surgeons regard fixation of the tumour as the chief contraindication to operation, it has often been pointed out that fixation of the rectum may be entirely due to inflammatory changes and that this fixation is often indistinguishable clinically from cancerous infiltration. In support of this view it is claimed that after colostomy has been performed the mobility of the rectum has been restored owing to the diminished irritation by septic material. It is stated in the report that there are no generally accepted criteria of operability and that each surgeon is guided largely by his personal experience and by the type of operation which he practises. Lockhart Mummery has shown that the perineal operation with a permanent colostomy when undertaken in suitable cases is associated with a mortality lower than that which follows the operation adopted by Miles. Readers are referred to an abstract of an article by Mummery published in this journal on June 18, 1927, and to an excellent article by Thring in the issue of February 28, 1925. Thring put the case for and against Miles's operation with clarity and fairness. It is not proposed to discuss the respective merits of these and other procedures, but merely to emphasize the fact that no definite rule can be laid down, but that every factor must be taken into consideration before an operation is undertaken. So much for operability as far as the surgeon is concerned. The stage which the disease has reached when the surgeon sees the patient, is dependent on the manifestation of symptoms. It has already been stated that the disease makes an insidious appearance. Herein lies the danger. Symptoms may be absent altogether until the growth has made considerable headway. Often, however, passage of blood occurs and the patient may think that he is suffering from hæmorrhoids. It is generally supposed that cancer of the rectum is associated with little pain, but according to this report such is not the case. Irregularity in the action of the bowel was most frequently the first symptom and the next was pain. The appearance of blood in the motions was third in order of appearance. The opinion is expressed that the early manifestation of pain justifies the view that education of the public may result in patients presenting themselves for treatment before the trouble has progressed too far. As a rule twelve months were allowed to elapse between the first symptoms and the performance of operation and when the patients presented themselves less than half of them were suitable for operation. The education of the public is of paramount importance and nothing can be done until the patient complains of some unusual manifestation. The education of medical practitioners is equally important. It happens not infrequently that a patient who complains of irregularity in bowel action, of vague abdominal pain and of losing weight, is subjected to examination by opaque meals and all the latest forms of X ray investigation, but a simple digital examination of the rectum is neglected. It must not be supposed that in these circumstances the medical attendant is deliberately emulating Naaman, the Syrian of olden times, who is reported as having scorned a simple remedy though he was quite willing to do "some great thing." Simple methods of examination are often forgotten. It is necessary to emphasize this point, for the adoption of a rectal examination in every abdominal condition will well repay the trouble taken, unexpected lesions will be discovered and the lives of not a few patients will be prolonged.

In regard to the results of operation, as revealed in this report, it is seen that one patient in every six died. The mortality was higher among those who were operated on at a late stage of the disease, but in spite of this two out of every five were alive three years later. These figures in all probability do not represent those which can be obtained at the present time, for the period investigated extends back as far as the 'eighties. The operative mortality is still fairly high, but operations are more radical than they were and the chances of survival are therefore greater. That the subject of cancer of the rectum demands the earnest consideration both of surgeons and general practitioners who as a rule have to recognize the condition, is shown by the following figures: During 1926, 5,700 persons in the Commonwealth died of malignant disease. Cancer of the peritoneum, intestine and rectum (the stomach is not included) caused the death of 855 persons; 442 of these were males and 413 were females.

Abstracts from Current Medical Literature.

PÆDIATRICS.

Carbohydrate Tolerance During "Insulin" Treatment.

K. U. TOVERUD (*The British Journal of Children's Diseases*, October-December, 1927) in discussing carbohydrate tolerance during "Insulin" treatment in diabetic children, points out the many factors which have to be taken into consideration. He studies the effect of these factors on a number of children (forty-seven), gauging their carbohydrate tolerance from time to time by the amount of "Insulin" necessary to keep the fasting blood sugar at a normal level and to keep the urine sugar-free. The first factor is the severity of the disease. A child in coma has a very low tolerance and a comparison of this with the tolerance in a later quiescent stage would not help to prove the value of "Insulin." The next factor is the control of the diet which must be such as to keep the urine sugar-free and the fasting blood sugar normal. If this is adhered to, it seems that the tolerance increases or at any rate remains stationary. On the other hand, the children who failed to adhere to the diet, rapidly became less tolerant and required greater quantities of "Insulin." A very important factor is that of infection. It was found that any of the upper respiratory infections or acute exanthemata greatly diminished the carbohydrate tolerance and out of seventeen in the series who succumbed, five died in coma closely connected with infections. Allen considers increased metabolic rate to be the cause. Wilder suggests the possibility of a toxic origin; the author favours the view that the acidosis present during most infections increases the "Insulin" requirement, probably owing to an increased glycogenolytic action in the liver and muscles. For this reason acute infections should be guarded against and attention should be paid to all possible foci of infection. The presence of acidosis in diabetes will greatly lower the tolerance. Muscular exercise in several instances caused "Insulin" shock, probably, as Allen explains, owing to the fact that the muscles make a better use of the "Insulin" or are able to metabolize with less "Insulin." Increase in body weight does not necessarily require an increased dosage of "Insulin." Of all these factors diet and infection proved to have the greatest effect on the tolerance. Those children who were kept free of infection and who were kept strictly to their appointed diet, were able to continue with the same amount of "Insulin" or in some instances with even less. Owing to the necessity for constant control and supervision and regular "Insulin" injections, the author strongly advocates institutional treatment. Three injections of "Insulin" per day are recommended and the diet is calculated on the basis of carbohydrate tolerance, and it is provided that there shall be a protein intake of three grammes per kilogram to children below seven years and two grammes above that age. The keto-antiketogenic ratio could not usually exceed 1·75 : 1 without the development of acidosis.

Cœliac Disease.

L. W. SAUER (*American Journal of Diseases of Children*, December, 1927) states that Howland in 1921 established a new era in the treatment of cœliac disease. The diet was divided into three stages: (i) Protein milk only, (ii) protein milk reinforced by almost pure protein foods, (iii) the gradual addition of carbohydrates. He quotes various authors who are convinced of the benefit of protein dietary. Fresh cow's milk is the worst food possible and this with carbohydrates and excess of fats plays an important rôle in the ætiology of the disease. Many hold that there is a congenital deficiency in gastric, intestinal or biliary secretions. Organisms have been isolated, but none has fulfilled Koch's postulates. The author favours the view that there is a specific causative agent and gives data which serve as circumstantial evidence, as follows: Cœliac disease has never been found in a breast-fed infant. Many are quite well until the prodromal period which usually occurs while they are on a mixed diet. Protein milk is unfavourable to the growth of intestinal organisms, hence the rapid improvement when it is given. The changes in the organs found *post mortem* are analogous to the changes found in various other chronic intestinal infections. If the proper diet is maintained, exacerbations do not occur, most probably because the causative organism has been eliminated. Cases of the disease have been reported in twins, sisters, cousins, nephews. The author reports three in which apparently the disease was transmitted.

Rheumatism, Chorea and Carditis.

R. MARSHALL (*Archives of Disease in Childhood*, February, 1928) reviews the histories of one hundred and eighty children who suffered from rheumatism, chorea and carditis. He divides them into groups as follows: (i) Those with rheumatism and carditis, (ii) those with limb pains, chorea and carditis, (iii) those with chorea, carditis and no limb pains, (iv) those with limb pains only and (v) those with chorea only. In the first group there were seventy-nine children, all of whom had suffered from rheumatic pains and twenty-six of whom gave a history of acute rheumatism. The average age at the first attendance was nine years and most of them were girls. Twenty-seven had had tonsillitis and eleven of these had had their tonsils removed apparently with benefit. Mitral regurgitation was present in forty-nine, mitral stenosis in eighteen and mitral and aortic lesions in nine. In all of these the valvular lesion was obvious on first examination and permanent damage had been done to the heart. There were nine patients with pericarditis and in all except one of them endocarditis was also present. Seventy-two were examined by the electrocardiograph. Of these thirty-three gave normal records. Nine had inversion of *T* wave in lead III. Two children with mitral stenosis and two with mitral regurgitation had right ventricular predominence and two of these died. Eleven had left ventricular predominence, four of them had aortic regurgitation, five mitral regurgitation and one pericarditis. Ten children with mitral involvement manifested notching of *P* wave. Only one of the seventy-nine children in this group had sinus arrhythmia. Of the seventy-nine, fifty-seven had a seriously damaged heart and nine had died. There were sixteen in the second group; all of them had evidence of carditis on the first examination and in seven the cardiac lesion had become progressively worse. Three had had recurrences of chorea and three a recurrence of slight pains in the limbs. Nine had had tonsillitis. Fourteen had severe cardiac lesions and two of these died. There were twenty-four placed in the third group. Nineteen of these had severe cardiac lesions and two died. All needed in-patient treatment. Mitral regurgitation was present in seventeen. The fourth group contained thirty-four children and the fifth group twenty-seven. Twenty-seven of these gave a history of tonsillitis. In some a transient apical systolic murmur was noted and sinus arrhythmia was present in fourteen. In many children with severe chorea carditis did not occur. A table is given showing the frequency of choreic attacks as follows: Forty-eight had one attack only, eleven had two, four had three, three had four and one had five. The author advocates prolonged treatment with sodium salicylate, interrupted occasionally by a course of the syrup of iron iodide. He recommends strongly that the public should be educated in the care of the rheumatic child, that notification should be made compulsory and that these children should be trained for some suitable occupation.

Non-Tuberculous Pulmonary Fibrosis.

C. D. S. AGASSIZ AND W. J. GILL (*Archives of Disease in Childhood*, February, 1928) have investigated a number of cases of non-tuberculous pulmonary fibrosis in children and have come to the following conclusions. The disease occurs in both sexes equally and may be found at any age, although the incidence in the series was greatest in children from five to ten years. There is no familial tendency. In the previous histories there was a high incidence of measles, whooping cough and pneumonia, the latter occurring in 60% of the cases investigated. Cough is the most frequent symptom and contrary to general opinion was found to be more frequent in the daytime and rarely spasmodic. The children are subject

to catarrhal attacks, especially in the winter months and the cough then becomes aggravated. Exertion or excitement may precipitate an attack. Expectoration is always very scanty and in the early stages thick, sticky and gelatinous. In later stages it becomes muco-purulent and when bronchiectasis occurs the typical sputum appears. In 40% of the series there was no complaint of dyspnœa. In more advanced cases dyspnœa may be evident on slight exertion or even at rest; but although this is apparent to the observer, it is rarely noticed by the child. Hæmoptysis rarely occurs, but there are occasionally streaks of blood in the sputum. Pain is seldom present and never severe. Cyanosis is one of the most constant signs of this disease and its degree depends on the extent of involvement. Its intensity is increased by exertion and in cold weather. Clubbing of the fingers is related to cyanosis and in 75% of the series these two signs were present together and were often accompanied by a coarseness of the features with some clubbing of the tip of the nose. The appearance and physique vary according to the stage of the disease. Physical examination of the chest reveals a diminution of expansion on the affected side and indrawing of the lower intercostal spaces. The heart may be displaced to the affected side. Vocal fremitus is usually diminished on the affected side and the percussion note is impaired, particularly at the base. Though one lung is usually more affected than the other, the disease is probably always bilateral. On auscultation there may be no adventitious sounds, though the breath sounds are usually diminished. More usually coarse and leathery dry râles are heard, especially at the base. Bronchial breathing may be present opposite the inferior border of the scapula. A characteristic of the disease is the variability of the extent and profuseness of the adventitious sounds. During pyrexial attacks the sounds become moister and more profuse, but very little evidence of bronchopneumonia is ever found. The temperature varies according to the activity or otherwise of the disease. The von Pirquet test yielded no reaction in 87% and the result was positive in 13%. The Wassermann test yielded a reaction in 8%. The blood oxygen content was found to be diminished in every instance. It was usually most diminished when cyanosis was most pronounced. In a typical case of extensive fibrosis the blood oxygen content was found to be 6·81 volumes %. In a patient with fibroid signs at both bases the result was 11·88 volumes %. In a child with no evidence of disease the result was 12·80 volumes % and in two children with pulmonary tuberculosis it was 12·40 and 13·40 volumes %. In two children with pulmonary tuberculosis superimposed on fibrosis the figures were 8·29 and 9·21 volumes %. These results are explained as follows. In pulmonary fibrosis the fibrosis involves the alveolar walls, it prevents the aeration of the blood which is still passing through the capillaries, and forms, as Lundsgaard and Van Slyke call it, an "unaerated shunt." In tuberculosis the blood vessels in the tuberculous deposit become thrombosed and thus the blood is prevented from circulating through the damaged alveoli and an "unaerated shunt" is avoided. Hence, when a cyanosed patient suffering from pulmonary fibrosis developes tuberculosis, the cyanosis diminishes in degree as the tuberculous process advances. The author describes the X ray appearances. The disease has to be diagnosed from tuberculosis, chronic bronchitis, pleural effusion, thickened pleura and bronchopneumonia. The differentiation from tuberculosis is important in view of the fact that the patients in this series were all sent to hospital with a diagnosis of pulmonary tuberculosis.

Thrombocytopœnic Purpura Hæmorrhagica.

M. S. REUBEN AND L. CLAMAN (*Archives of Pediatrics*, February, 1928) report a case of thrombocytopœnic *purpura hæmorrhagica* in which they claim that splenectomy saved the life of the child. Thrombocytopœnia, in their opinion, is a derangement of the reticulo-endothelial system whose duty it is to catabolize dead corpuscles and platelets. The cells of this system are found in the lymph sinuses, the blood sinuses of the spleen, the capillaries of the liver lobules, bone marrow, connective tissue (wandering cells) and in contact with the capillaries as Rouget cells. They describe the discovery of platelets and of the fact that their reduction below a certain level is related to the hæmorrhagic tendency. Burke and Tait have shown that coagulation is dependent on the platelets and Lee and Minot have further shown that clot retraction depends on the number of platelets which are not used up during coagulation. Thrombocytopœnia is characterized by a definite diminution of the platelets and it is a matter of doubt whether this is due to a failure of the constructive properties of the marrow or to an overactivity of the destructive properties of the reticulo-endothelial system. Frank's theory that the spleen exerts in this condition some inhibitory action on the formation of platelets led to splenectomy. The authors believe that in *purpura hæmorrhagica* there is a toxin formed in the spleen which increases its thrombolytic power, causes the megacaryocytes to produce less platelets, affects the quality of the platelets and alters the Rouget cells so that the capillaries become more permeable. Splenectomy is followed by a rise in the platelet count. A rise may also be brought about by transfusion, the injection of protein or injections of adrenalin, but the effect is transitory. Spleneetomy causes a more persistent rise. The authors give details from the literature of twenty-one patients suffering from the chronic type for whom splenectomy was performed. Of these one died, nineteen were improved and in one there were slight recurrences of epistaxis and petechiæ. After splenectomy the bleeding time returned to normal, clot retraction became normal, hæmorrhages ceased and in most patients there was a definite rise in blood platelets with a subsequent fall from within two days to five months afterwards to a normal or subnormal level without return of hæmorrhages. Of eight patients operated upon in the acute stage, seven died; but the authors consider the data insufficient to justify the assertion that splenectomy is contraindicated in the acute form of the disease. They quote the history of a patient of their own suffering from the acute type, whose life was undoubtedly saved by splenectomy. The patient was free from symptoms eighteen months after the operation. They advise that every means should be used to stop hæmorrhage and to build up the patient before operation; but if the bleeding continues, transfusion should be followed by splenectomy, regardless of whether the condition is acute or chronic.

Endocarditis.

M. S. REUBEN (*Archives of Pediatrics*, February, 1928) differentiates subacute bacterial endocarditis from other forms of endocarditis met with in children. In tracing the evolution of valvular disease, he notes the close relationship between endocarditis and the existence of musculature and blood vessels in the valves. In the fœtus the valves are more vascular on the right side and endocarditis is more frequent on that side. In the adult endocarditis is most frequently found in the aortic cusp of the mitral valve and this cusp is the last to lose its musculature. The author states that endocarditis in the first two years of life is generally associated with septic rather than rheumatic infection and *vice versa* after that age. Geiger has collected records of ninety children who suffered from endocarditis; thirty of these were under two years and the condition of eleven of them was due to sepsis and of one to rheumatism. The author, however, points out that, though it is unusual to find a rheumatic endocarditis in a child under two years of age, it is not unknown even in earliest infancy. Rheumatic heart disease affects primarily the myocardium and early murmurs are usually due to dilatation, not to endocarditis. Skiagrams of the heart in acute rheumatism have consistently revealed an increased cardiac shadow. This returns to normal if the cause has been dilatation, but persists when endocarditis or pericarditis is present. The rheumatic virus tends to affect all layers of the heart and is the commonest cause of pleurisy with effusion in children. A secondary invasion of the blood stream by streptococci occurred in 10% of the cases; the blood cultures were usually sterile. The pathognomic lesions of rheumatism are the Aschoff bodies and cutaneous

nodules. The mode of onset of rheumatic endocarditis is very insidious and a fully developed valvular disease may be present as the result of a previous unrecognized endocarditis. Acute bacterial endocarditis may be caused by many organisms, but usually by the *Streptococcus hæmolyticus*. It seldom affects normal valves, but elects those previously damaged or congenitally defective. The endocardium becomes ulcerated and necrosed and covered with blood platelet masses which become invaded by organisms and polymorpho-nuclear cells. Purulent pericarditis may occur and petechiæ and hæmorrhages are frequent. It is an acute and fatal disease and the duration is one to six weeks. Subacute bacterial endocarditis is a true endocarditis. The disease affects the endocardium primarily, while the myocardium retains its normal functional capacity for months. In 95% of cases the causal organism is the *Streptococcus viridans* and occasionally *Bacillus influenzæ* or gonococcus, but practically never the *Streptococcus hæmolyticus*. It generally affects damaged valves and a focus of infection is usually found in sinuses, teeth, tonsils, intestines, bronchi or lungs. The right side of the heart is seldom involved. Pericarditis seldom occurs. The endocardium is not purulent, the vegetations containing very few polymorpho-nuclear cells, but large numbers of organisms and there is little tendency to ulceration. Giant cells may be present and are characteristic of this disease. Osler gives the following as the most suggestive symptoms: A knowledge of the existence of an old valvular lesion, (ii) the occurrence of embolic features, (iii) the onset of special skin signs (purpura and Osler's nodes), (iv) progressive cardiac changes, (v) growth of organisms in blood culture.

Gelatine as an Accessory Infant Food.

H. H. PERLMAN (*Archives of Pediatrics*, January, 1928) studies the value of gelatine as an accessory infant food. For the experiments half a teaspoon of powdered gelatine was added to the day's feeding for infants under six months and one teaspoonful for infants over that age. The gelatine was added to thirty cubic centimetres (one ounce) of cold milk and allowed to soak for ten minutes. The same quantity of hot milk was then added, while the mixture was stirred until the gelatine was completely dissolved. The gelatinized milk was then added to the remainder of the day's feeding, the whole mixed thoroughly and kept on ice. Eight babies under a year and ten between one and two years were fed on gelatinized milk. There were eighteen controls, seventeen of which were under one year and one aged sixteen months. The babies fed with gelatine gained on an average 173·6 grammes (6·1 ounces) a week as against 118·8 grammes (4·2 ounces) in the controls. Regurgitation seldom occurred, there was no vomiting and the motions were normal. The author concludes that gelatinized milk is superior to whole milk dilutions as a means of increasing weights in malnourished infants.

The Thymic Syndrome.

J. H. WEST (*Archives of Pediatrics*, January, 1928) discusses the so-called thymic syndrome in children. The typical thymic child is overweight, pale and flabby, is prone to attacks of breath-holding and suffers from simple cyanosis, noisy dyspnœic breathing and convulsions similar to those of tetany. These symptoms are often found in the presence of an enlarged thymus and have been variously explained as due to pressure and intoxication. X rays have made the diagnosis of enlarged thymus possible by a skilled radiologist. Kerley considers a thymus enlarged if the shadow exceeds one and a half times the diameter of the spine at the level of the third thoracic vertebra. In view of the fact that sudden death may follow trivial causes in these patients, the author considers it advisable to ascertain the presence or otherwise of an enlarged thymus before submitting babies or young children to any operative procedure. The treatment by means of X rays, while purely empirical, has proved very generally successful in improving the symptoms and diminishing the thymic shadow.

Hæmorrhagia Neonatorum.

R. J. BEVERIDGE (*Archives of Disease in Childhood*, February, 1928) studies a number of cases of *hæmorrhagia neonatorum*. She finds that the onset of the bleeding is most frequent between the second and the fifth day and that this corresponds to the period when the coagulation time of the blood is most prolonged in infants. Eighteen of the twenty-four children studied had normal births and were apparently normal infants. In the vast majority the bleeding took place in the alimentary tract, from the umbilicus or from the skin. The most satisfactory treatment was found to be the injection of whole human blood and in severe cases transfusion.

ORTHOPÆDIC SURGERY.

Tuberculosis of the Hip.

ALAN DE FOREST SMITH AND WIN H. WATTERS (*Journal of the American Medical Association*, January 21, 1928) review the end results of 208 patients treated for tuberculosis of the hip with the Taylor traction hip splint and heliotherapy during seventeen years. They considered that in forty-six of these cases there was a lack of evidence that the patient had a tuberculous infection and point out that nowadays no joint is treated for tuberculosis in their clinic until the diagnosis has been proved, either by aspiration and guinea pig inoculation or by exploratory operation. Twelve of the remainder were under observation for three years at least and are omitted from the final consideration because they consider that studies of patients under observation for less than five years are of little value. Of the remaining 150 patients 36 died, in 71 the disease was still active and in 41 it was quiescent, with varying degrees of deformity and with definitely limited motion or no motion. There was a striking tendency to relapse even after long periods of quiescence. The authors comment on the excellent general physical condition of these patients even when they had progressive destruction of the hip joints. Nine patients have had hip fusion performed and those no longer in a cast are free from symptoms. Only two patients were free from symptoms and had a useful range of motion in the joint.

Penetrating Wounds of the Knee Joint.

F. MANDL (*Wiener Medizinische Wochenschrift*, January 28, 1928) discusses the treatment of penetrating wounds of the knee joint. The majority occurs with wood workers and butchers or as the result of street accidents. Every wound must be carefully traced even if it means opening up the track to determine whether the joint has been penetrated. In such cases the skin wound, the track and the opening in the capsule should be excised. The joint cavity is then filled with an antiseptic solution composed of liquid carbolic acid thirty cubic centimetres, camphor sixty grammes, absolute alcohol ten cubic centimetres. The capsule is then closed and the skin is sutured. Infected joints are treated by making a small incision to drain the pus, the cavity is flushed with the solution already mentioned and two glass drains are inserted and plugged. If within twenty-four to forty-eight hours both temperature and pain have subsided, the drains are removed; if not, then further irrigation is done. Of seven cases in which the prophylactic operation was performed, a good functional result was obtained in six. Eight joints with severe infection resulted in four with good movement, some restriction occurred in one instance and ankylosis in three. The average duration in hospital was forty-six days for those patients who recovered the function of the joint as compared with eighty-eight days for those whose joints became ankylosed.

Derangements of the Coccyx.

PHILIP LEWIN (*Surgery, Gynecology and Obstetrics*, November, 1927) describes the derangements of the coccyx. After giving a description of the anatomy including muscular attachments and nerve supply, he enunciates the clinical disturbances in their order of importance, dislocation, ankylosis, tumours and disease. The chief symptom of dislocation is pain which is especially troublesome when the patient is sitting on a soft

surface. In the majority of instances X rays give no help in the diagnosis, but rectal examination is of the greatest value. Many of these patients also have lumbo-sacral arthritis and this condition is not cured by treatment of the coccydynia. Where necessary the author makes a median incision and removes the bone at the sacro-coccygeal joint without disturbance of the muscular attachments.

Spasmodic Torticollis.

C. W. MAYO (*Proceedings of the Staff Meetings of the Mayo Clinic*, November 16, 1927) reports a case of spasmodic torticollis in a patient whose tonsils were found to be enlarged and one of whose teeth was periapically infected. The infected tonsils and tooth were removed, Rosenow cultured them on blood agar and in glucose brain broth and recovered *Streptococcus viridans*. He injected this culture into the brain of a rabbit and obtained symptoms of acute encephalitis which subsided in a few days, and the animal was then apparently well except that the signs of spasmodic torticollis became steadily worse and persisted up to the date of the report seven weeks after injection. Intracerebral inoculation of the culture from the abscess of the tooth produced no effect on the rabbit, although the culture contained large numbers of colonies of *Streptococcus viridans*.

Studies in Basal Metabolism in Chronic Arthritis.

LORING T. SWAIM AND LOUIS M. SPEAR (*The Boston Medical and Surgical Journal*, September 1, 1927) have made a study of the basal metabolism in chronic arthritis and for this purpose have adopted the classification used by Goldthwait, Painter and Osgood. According to this classification there are three forms of chronic arthritis, infectious, atrophic and hypertrophic arthritis, the first being considered as a periarticular inflammation with very little bony change. The second is one in which the bone changes predominate over the soft tissue changes and are characterized chiefly by bony atrophy, destruction of cartilage and decalcification of the bones, not only about the joint but through the whole body. The third type was characterized by very little soft tissue change, but by great increase in bony overgrowth and thickening of the structure of the bone as revealed by X rays. The authors studied two hundred patients, one hundred and forty-two of whom were between twenty-one and sixty years of age. The infectious and atrophic types occurred in early and middle life and the hypertrophic at a later age. Of the patients 26% were males and 74% females. The authors found that the basal metabolism of some patients with an increased basal metabolism has after the administration of thyreoid extract, dropped below normal and as thyreoid extract has been increased the metabolism has gradually risen again towards normal with a distinct improvement in the physical condition and a large improvement in the arthritis. They consider that this improvement is not due alone to rest and hospital treatment, because the basal metabolism of some patients who were given this routine without thyreoid extract, dropped to a lower level, but did not increase to a higher rate until the thyreoid had been used. The general tone of the body was improved only after thyreoid medication.

Fracture of Tarsal Scaphoid.

EDWIN P. LEHMAN AND I. H. ESKELES (*Journal of Bone and Joint Surgery*, January, 1928) describe several cases of fracture of the tarsal scaphoid and suggest that these fractures from indirect violence are generally accompanied by laceration of the dorsal scapho-cuneiform ligament. There is forced flexion of the foot at the medial tarsal joint and in this position the scaphoid is driven against the upturned sharp inferior proximal angle of the middle cuneiform bone and the fracture results.

The Periosteum in Fractures.

BEVERIDGE H. MOORE (*Journal of Bone and Joint Surgery*, January, 1928) has conducted some experiments with tibiæ of calves to investigate the rôle of the periosteum in recent fractures and he concludes that the elastic pull of the periosteum is an additional factor to muscle pull in producing angular and overriding deformity. It also tends to cause angular deformity, if reduction is not anatomically perfect. But when anatomically perfect reduction is obtained, the elastic action of the periosteum tends to maintain it.

Treatment of Ankle and Leg Fractures by the "Delbet" Ambulatory Plaster Splint.

E. LESLIE ROBERT (*The British Journal of Surgery*, January, 1928) describes the treatment of ankle and leg fractures by the "Delbet" ambulatory plaster splint. He holds that the use of the "Delbet" plaster makes the period of treatment considerably shorter compared with other methods and that it disposes of the tedious and expensive course of physical therapy required by them. In fractures of the leg he concludes that actual anatomical restoration is not essential in order to regain perfect function, provided that angulation and shortening of more than 2·5 centimetres (one inch) are corrected. He also finds that full weight transmission through the seat of fracture made possible by using the "Delbet" plaster, stimulates rapid formation of strong callus and so shortens the period of treatment. He describes the method of applying the plaster in detail. Briefly it consists of a band of plaster five centimetres (two inches) wide down each side of the leg. These are fixed by a stirrup-shaped band of plaster holding the ankle and heel firmly and the ends extend up spirally round the limb. The upper ends of the bands of plaster are fixed by a transverse band just below the tubercle of the tibia. The patient is allowed to walk on this plaster with the aid of a stick in a few weeks and active movements at the ankle joint are encouraged.

Fracture of the Os Calcis.

PHILIP D. WILSON (*The Journal of the American Medical Association*, November 12, 1927) found involvement of the calcaneo-astragaloid joint with serious articular deformity in thirty-four out of thirty-eight consecutive fractures of the *os calcis*. He emphasizes the fact that it is impossible to secure adequate replacement of the fractured portions without some form of open operation. He strongly recommends arthrodesis of the subastragalar joint, performed through an incision over the lateral surface of the joint. Latterly he has performed arthrodesis of the mediotarsal joint as well and thinks the results are better with the latter procedure. He immobilizes the foot in plaster in a good weight-bearing position for eight weeks and permits the patient to bear weight in the plaster at the end of six weeks. As soon as the plaster is removed, the arch is supported by a well fitting plate and the use of the foot is encouraged.

Treatment of Spinal Conditions, Notably Scoliosis.

CHARLES LE ROY LOWMAN (*Journal of Bone and Joint Surgery*, January, 1928) describes his results over a period of five years in the treatment of scoliosis by the "continuous traction method." He uses a head halter and raises the head of the bed ten centimetres (four inches). The height is increased by five centimetres (two inches) every few weeks until it is twenty to twenty-five centimetres (eight or ten inches) above the floor. In the meantime manual corrections, breathing exercises, passive stretching and massage over the weakened muscles of the convexities are given their adequate place in the treatment and the author pays particular attention to the presence of anæmia and acidosis. He maintains that continuous traction from four to eight weeks will accomplish as much as the first six months of "cast treatment." It is sometimes necessary to use casts or braces or spinal fusion for final control of the scoliosis, but even in these circumstances the patients are much more comfortable while awaiting final treatment.

Dislocation of the Head of the Radius.

HENRY MILCH (*Journal of Bone and Joint Surgery*, January, 1928) describes an operative procedure for treating dislocation of the head of the radius without excising the head of the bone. It consists in placing a strip of *fascia lata* around the head of the radius from the epicondyle of the humerus to the neck of the radius and passing the ends of this strip through drill holes in the head of the ulna. The ends are then tied and sutured to the periosteum.

Special Abstract.

STATUS LYMPHATICUS.

To many medical practitioners the term *status lymphaticus* conveys little. When an unexpected death occurs under chloroform anæsthesia, the name is used and, like "the blessed word Mesopotamia," it brings a certain amount of comfort. As a matter of fact among those who have studied the subject, there is no agreement in regard to its nature. Some writers have gone so far as to declare that as a separate entity it is a myth. Others have identified it solely with a disorder of the thymus gland, but the majority regards it as a grave disorder dependent on incoordinated action of more than one structure in the body and capable of exercising malign influence on the health of the individual. A general review of the subject has recently been made by David Marine[1] in so excellent a manner that the following *résumé* has been prepared for the benefit of Australian practitioners.

Historical.

Marine starts by stating that in 1614 Felix Plater reported the sudden death without obvious cause of a boy in whom an enlarged thymus was found at autopsy. In 1830 Kopp advanced the view that laryngospasm was a true thymic asthma due to the pressure of the enlarged thymus on the trachea, great vessels or autonomic nerve trunks. In 1858 Friedleben published the results of his researches and asserted that pressure from an enlarged thymus could not explain Kopp's *asthma thymicum*. Many of Friedleben's conclusions are still sound, such, for example, as his view that the thymus may be congenitally absent or experimentally removed without detectable impairment of health and that it may have an obscure influence on the nutrition of the osseous system. The next important contributions to the subject were made in 1889 by Arnold Paltauf who advanced the view that "thymus death" was due to a lowered resistance, dependent on a specific constitutional anomaly of a lymphatic chlorotic type, which so weakened the influence of the nervous system that persons with this anomaly were unable to withstand shocks or injuries that would not have seriously affected normal persons. He believed that the anatomical changes observed were only the gross manifestations of the nutritional defect or anomaly which he designated *status lymphaticus*.

Terminology.

Among the terms used to describe this specific constitutional defect are: laryngismus, *asthma thymicum*, *stridor thymicum*, *mors thymica*, *status lymphaticus*, *constitutio lymphatica*, *status thymico-lymphaticus*, *status thymicus* and *status hypoplasticus*. Some observers hold that these names indicate slightly or distinctly different pathological states. Marine does not believe that there is at present any basis for this separation. All the facts in his opinion indicate that these terms are descriptive of the different degrees, the different manifestations and the different stages of fundamentally the same physiological defect occurring at different ages. He defines *status lymphaticus* as a constitutional defect, usually congenital (though it may be acquired) dependent on an inadequacy of some function of the suprarenals, sex glands and autonomic nervous system and associated with lowered resistance or increased susceptibility to a great variety of non-specific, physical and chemical agents.

Anatomy and Physiology of the Thymus.

It has been pointed out already that the thymus is considered by many to be the central feature of *status lymphaticus*. For this reason Marine devotes considerable space to a summary of the anatomy of this organ in the belief that this will be useful in "evaluating its importance in the essential and more detailed manifestations of this constitutional defect."

The thymus developes as a pair of structures from the entoderm of the third and fourth branchial arches in close association with the corresponding parathyreoids. According to Hammar the epithelial character of the thymus is evident until the end of the second month of intrauterine life. At this stage the cells become more loosely arranged and give off protoplasmic processes which anastomose to form the reticulum. Divergent views are held in regard to the development beyond this stage. According to the most popular belief at the present time the reticulum and Hassall's corpuscles are the only elements developed from the original epithelial *Anlage*, while the small thymic cells (lymphocytes) and eosinophile cells arise from mesenchymal cells that have migrated into the epithelial structure from surrounding tissues, and it is also held that further development of the thymus is that of a true lymphoid tissue. Although the small thymic cells and true lymphocytes resemble one another in their morphological characteristics, in their susceptibility to injury by X rays, in their serological reactions, in having amœboid movements and in their general pathological behaviour, there is still a basis for doubt that the thymic cells are true lymphocytes.

It is generally agreed that the absolute weight of the thymus increases rapidly up till the end of the second year of life and then changes but little until the seventh year, when it again increases slightly to fall off again about the eleventh year. The thymus is larger in the male during the first four years of life; it remains approximately equal in the two sexes until the eleventh year and after this it is larger in the female. By the term age involution is meant the normal atrophy of the thymus which sets in at the age of puberty and continues throughout old age. Waldeyer in 1890 disposed of the view that the thymus disappears in old age. There is no definite distinguishing feature between the age involution and the pathological and accidental involution due to disease. The two types of involution may occur simultaneously and accidental involution followed by regeneration must occur in most persons one or more times before the normal involution sets in. Why sexual maturity should mark the turning point in the size of the thymus is not known. It has been claimed that the sex glands play a decisive rôle in initiating this anatomical and physiological decline of the organ. There is abundant evidence, however, to show that the cause is a far more complex culmination of the interactions of the glands of internal secretion and at least involves the thyreoid, suprarenals and sex glands. After sexual maturity there is rapid reduction in the volume of the parenchyma for the first four or five years, largely due to a decrease in the small thymic cells; then reduction becomes more and more gradual. The decrease in the volume of the medulla occurs at a later stage and is due in part to a decrease in the rate of the division of the reticular cells and in part to their actual disintegration.

Accidental or pathological involution differs from normal involution in that it occurs rapidly and at any age. It is seen in all animals and apparently under a great variety of conditions, such as acute and chronic infections, various intoxications, acute and chronic inanition, after X ray injury and during pregnancy. Regeneration may occur after pathological involution.

The function of the thymus is unknown. It closely resembles the lymphoid tissues in its principal physiological and pathological reactions and most investigators associate it with those tissues. There is no proof that it has an internal secretion. Its behaviour indicates that it plays some important rôle in the maintenance of normal nutrition, at least during the period of growth up to sexual maturity. It is not essential to life. Marine gives a short account of the results of experimental work on the thymus by many workers. The conclusions are many and varied and touch on such subjects as the ossification of bones, calcium metabolism, the diminution of the virulence of bacteria and the neutralization of their toxins, the stimulation of phagocytosis. He points out that many of the conclusions cannot be accepted on account of the difficulty of complete removal of the thymus. All observers are agreed that the thymus is an important source of blood lymphocytes and possibly of eosinophile cells and the most prominent physiological features concern the interrelations of the thymus with the sex glands, the thyreoid and the suprarenals.

[1] *Archives of Pathology*, April, 1928.

Pathological Anatomy of Status Lymphaticus.

Marine accepts the view, expressed by many authors, that there is not a known disease entity in which the thymus occupies the central or causal rôle. On the other hand he believes that *status lymphaticus* or *status hypoplasticus* is a clinical and pathological entity the chief physiological characteristic of which is lowered resistance and in which hypertrophy and hyperplasia of the lymphoblastic tissues is a frequent anatomical manifestation. He states that Greenwood and Wood have expressed the view that it is as accurate to attribute cause of death to "the visitation of God" as to *status lymphaticus*. In his opinion these authors have laid too great stress on the thymus and have overlooked the essential feature of Paltauf's conception. It is of secondary importance whether the thymus is large or small, since the thymic change indicates only the stage or degree of the individual's lymphoid reaction at the time. If it be assumed that *status lymphaticus* is a nutritional defect or deficiency disease tending towards spontaneous recovery and manifesting itself at different ages, it follows that there are all degrees of the condition, mild and severe, and all stages, progressive and regressive. Marine is therefore content to catalogue the lesions in the order of their prominence and constancy and he points out that a great deal must be omitted which may be of significance in the tissues.

The Thymus.

The thymus gland is usually found to be larger than it should be for the particular age of the individual. The size and weight, however, must be controlled by a microscopical determination of the amount of lymphoid tissue present. The prevailing opinion is that there is no essential histological difference between the usual thymus of *status lymphaticus* and that of a normal child. Schridde, however, believed that hyperplasia of the medulla is fairly characteristic, while the cortex may be atrophic or of normal thickness.

The Spleen.

The spleen is as a rule moderately enlarged, often to such a degree that it may be palpated. The malphigian bodies are prominent and the endothelial elements have been found hyperplastic.

The Lymphatic Glands.

Hypertrophy and hyperplasia of the lymphatic glands and of the lymphoid tissues of the various organs are present. There are wide variations in the degree of enlargement of the lymphatic glands. The glands most prominently involved are those of the pharynx, thorax and abdomen. Adenoids are usually present. The lingual and faucial tonsils are nearly always enlarged and Schridde lays great stress on hypertrophy of the lingual lymphoid tissue as being of diagnostic importance. Occasionally fibrosis and exhaustion atrophy of the lymphatic glands are present. These represent the end stage of an ineffectual compensatory hypertrophy. Collections of lymphoid cells are found in such organs as the liver, the kidneys, the skeletal muscles and particularly the thyreoid. Changes are often present in the bone marrow; some observers have described in the marrow true lymphatic glands with germinal centres. The view that the thymus and the lymphatic glands are complementary has been suggested by Marfan and Warthin as a possible explanation of the fact that hypertrophy of the thymus may be present with fibrotic lymphatic glands and spleen and that both the thymus and lymphatic glands may be hyperplastic or that the lymph glands may remain hyperplastic after involution of the thymus.

The Reticulo-Endothelial System.

Few studies have been made on the relationship of the reticulo-endothelial system to *status lymphaticus*. Aschoff is inclined to view the entire lymphoid hyperplasia as a specific reaction of the reticulo-endothelial system. Marine thinks that in view of the relationship of the lymphoid and hæmatopoietic tissues to the defensive mechanism of the body, further studies on the reticulo-endothelial system are likely to yield additional data on the nature of *status lymphaticus*.

The Thyreoid Gland.

The condition of the thyreoid gland in *status lymphaticus* varies according to the endemicity of goître in the place of residence of the patient. The stroma of affected glands is usually somewhat increased and this indicates a prolonged struggle; the gland at the time of examination may be actively hyperplastic or involuted. There is abundant experimental evidence that the thyreoid is intimately associated with the thymus and lymphoid tissue. Apart from the physiological antagonism indicated by the experimental data the significance of thyreoid enlargement in *status lymphaticus* is unknown.

The Suprarenals.

The suprarenals in *status lymphaticus* may be small and the chromaffin tissue as well as the cortex may be strikingly reduced. Wiesel associates this hypoplasia of the chromaffin system with the cardio-vascular changes, the low blood pressure and the increased vagus tone. He also assumes a close relationship between *status lymphaticus* and Addison's disease. Marine points out that there is experimental evidence to support this view. Since suprarenalectomy, performed on rats and rabbits, causes a lowering of resistance and thymic regeneration, it is probable that the spontaneous involution of the human suprarenal cortex which begins during the second week of extrauterine life, may be a causal factor in the hypertrophy of the thymus and of the lymphatic glands and in the lowered resistance in infants. The destructive degeneration of the suprarenal cortex seen in man apparently does not occur in animals and it is possible that for this reason *status lymphaticus* is rare in animals.

The Sexual Organs.

No definite changes in the sexual organs associated with *status lymphaticus* have been observed and as most fatal cases occur in children, morphological changes in the sex gland would be difficult to recognize.

The Cardio-vascular System.

In patients with *status lymphaticus*, examined after puberty, hypoplasia of the heart and of the large arteries has been prominently mentioned since Virchow first called attention to the occurrence of this abnormality in the chlorotic and lymphatic constitutions. The underdevelopment of the cardio-vascular system may be primary, but in most instances it seems more logical to assume that it is secondary to the general asthenia and low blood pressure; as Hart has pointed out, it does not appear to have any general pathological significance.

The Nervous System.

Anatomical changes of note have not been described in the central nervous system, although there is abundant evidence of serious functional derangement.

The Osseous System.

Disturbances in calcification have been prominently associated with *status lymphaticus* from the beginning. A considerable number of children with *status lymphaticus* manifest more or less pronounced evidence of rickets. Now that the pathogenesis of rickets is better understood as a deficiency disease and in view of its close association with *status lymphaticus*, Marine believes that the work on rickets may indicate the direction which research should take in the further study of the nutritional defect underlying *status lymphaticus*. In other words there may be a vitamin insufficiency in addition to a hormonal insufficiency.

Gross Anatomical Changes.

A relative lymphocytosis is usually present and is in general proportional to the prominence of the lymphoid tissue. The fœtal lobulations of the kidney are often preserved, as is also the infantile type of appendix and caecum. The skin as a rule is velvety, the hair decreased and the subcutaneous fat well preserved.

Association with Other Diseases.

Recent studies indicate that thymic enlargement is present in practically all cases of primary exophthalmic goitre. Prominence of the lymphoid tissues and thymus is also frequently observed in Addison's disease and in chlorosis. Since sufficient injury of the suprarenals will cause regeneration of the thymus, it is evident that a close relationship must exist both ætiologically and pathologically between exophthalmic goitre, Addison's disease and chlorosis. Ohlmacher has emphasized the association of idiopathic epilepsy and *status lymphaticus* and there is some evidence of a relationship between the latter and asthma, hay fever and eczema, at any rate in children.

Lowered Resistance.

The close relationship between *status lymphaticus* and lowered resistance or increased susceptibility is the most prominent known clinical manifestation both of *status lymphaticus* in man and of that condition produced experimentally in animals. The lowering of resistance is not specific, for it can be demonstrated with a great variety of physical and chemical agents. Drugs occupy the most prominent place as a cause of death of persons with *status lymphaticus*.

Of all drugs anæsthetics are mostly frequently mentioned in the literature and chloroform heads the list. Blake, however, has shown that all anæsthetics are dangerous. Anæsthetics are also dangerous in exophthalmic goître, Addison's disease and chlorosis and this is another of the many indications of a close biological relationship between these diseases. Marine refers to the occurrence of sudden death after the subcutaneous administration of serum and to deaths following trivial surgical and medical procedure. He states that deaths in the latter circumstances are difficult to explain without the assumption of a deleterious hypersusceptibility to psychical and physical shock. Some observers have suggested that in cases of *status lymphaticus* death is due to anaphylaxis; but anaphylaxis would account for only a small proportion of these fatalities, since death occurs after the injection of non-protein material as well. The cause of death is more mysterious and deep-seated. Marine thinks that one of the vital factors involved is touched by the view of Wiesel, that it is due to the injurious raising of the vagus tone in association with insufficiency of the chromaffin and sympathetic nervous system.

Marine points out that there is surprisingly little literature on the question of hypersusceptibility to infection in patients with *status lymphaticus* and that this condition does not figure so prominently as it deserves in the conception of the factors which determine the prognosis in acute infections. At the same time he refers to numerous deaths in various conditions in which *status lymphaticus* was regarded as being responsible. It is known that suprarenalectomy causes the greatest lowering of resistance or increase in susceptibility of any known experimental procedure and in view of the knowledge that suprarenalectomy causes a true experimental *status lymphaticus*, the conclusion appears justified that a deficiency of some suprarenal or gonadal function is a major factor in the ætiology of *status lymphaticus* and in the lowered resistance seen both in the spontaneous and in the experimentally produced lymphatic state.

Clinical Diagnosis of Status Lymphaticus.

The greatest need in connexion with *status lymphaticus* is the discovery of constant and characteristic symptoms and signs which the clinician can recognize on routine examination. The search for such criteria is beset with great difficulties. The greatest difficulty is that normally the lymphoid tissues are prominent in infants and in children. The other difficulties which Marine sees are that all degrees of *status lymphaticus* exist, so that it is not possible to distinguish the normal from the abnormal, even after the age of puberty; that spontaneous recovery tends to occur as age advances and that the syndrome may be acquired. The last mentioned statement is held to be proven because the condition is readily reproduced experimentally in certain animals.

The usual signs of a pale, thin, velvety skin, enlarged tonsils, superficial lymphatic glands, the thymus and lymphocytosis are not constant occurrences. Schridde believes that when the lingual follicles are enlarged careful search should be made for other signs. Marine is of the opinion that in view of the present conception of the physiological defect underlying *status lymphaticus*, it is not likely that tissues with so great a capacity for rapid hyperplasia and equally rapid involution as the thymus and the lymphatic glands will show morphological evidence of specific diagnostic importance in this constitutional anomaly. It would be more logical to discover some tests of resistance or susceptibility that could be applied clinically. The systemic or the dermal reaction to some drug or toxin should be sought in the hope of finding one that would produce a characteristic reaction without being dangerous in small doses. Epinephrine, as used in the Goetsch test, or "Insulin" are examples of drugs that might be used.

The Cause of Death in Status Lymphaticus.

Several views have been put forward to explain the cause of death in *status lymphaticus*. According to one, death is due to pressure of an enlarged thymus on the trachea, blood vessels and nerve trunks. According to another, it is a result of the constitutional defect manifesting itself through an injurious raising of the vagus tone, together with a deficiency of the chromaffin system and weakness of the sympathetic system. Another view is that it results from hypersusceptibility to physical and chemical agents. Anaphylaxis is responsible according to a fourth view and a fifth is that it results from an abnormal thymus secretion and a general lymphotoxæmia. Although in occasional instances an enlarged thymus may cause tracheostenosis and other symptoms, it must be concluded that in the great majority of cases no clinical or *post mortem* evidence exists that death is caused by compression and that the explanation of thymic asthma or thymic death is not so simple or at least that pressure effects are inadequate in the absence of a constitutional predisposition to account for death. The immediate cause of death in so-called thymic asthma is stoppage of the heart. It has been assumed in this connexion that there is a neurosis of some sort in which hyperexcitability of the vagus coupled with a weakness of the sympathetic, an autonomic imbalance, is present and is the basis of the cardiac stoppage. In regard to anaphylaxis it does not appear that it is of greater importance than many other factors which lead to sudden death, but rather that it is an additional means of demonstrating lowered resistance. The postulation of a lymphotoxæmia has in its support only the relatively constant pathological condition of lymphoid and thymus hyperplasia.

Marine is of the opinion that a promising lead is offered by the observations of MacLean and Sullivan who found the blood sugar definitely lowered in three cases of *status lymphaticus* in infants and associated in "Insulin"-like convulsions. These observers interpret their results as further support of the hypothesis of suprarenal insufficiency as the cause of *status lymphaticus*, in other words a lack of the antagonistic action of epinephrine. Hypoglycæmia has also been noted in other conditions closely related to *status lymphaticus*, for example, in exophthalmic goître and in Addison's disease and following suprarenalectomy in animals.

Correspondence.

AN UNUSUAL EPIDEMIC.

SIR: Dr. Nimmo, of Narrandera, writes in the journal of May 5, 1928, reporting an unusual epidemic.

This epidemic occurred in this town also, but started here about six weeks prior to the date Dr. Nimmo reported.

It commenced when a traveller arrived from Queensland and during his stay here I treated him for a typical attack of dengue fever. During that time and the following three months we suffered from a plague of mosquitoes. The epidemic was easily traced from the first case spreading in a gradually increasing circle.

Dr. Nimmo gives a very good description of the condition, except regarding the swelling of the joints. There was no actual swelling of the joints or fluid in them. It was all periarthritic.

I have no doubt that the epidemic was dengue. The average case was not typical, but about one case in five or six gave a typical picture of dengue fever.

During the epidemic I tried to collect a specimen of the mosquito *Stegomyia fasciata*, but was unable to definitely distinguish it. However, from the number of mosquitoes I examined I was able to definitely recognize two specimens of *Anopheles*.

Yours, etc.,

A. M. EDWARDS.

"Yaamba," Pine Street,
Hay, New South Wales.
May 12, 1928.

"ATOPHAN."

SIR: Is "Atophan" a safe drug? In asking this question I would add a further one: Should chemists provide the public with "Atophan" tablets as they do aspirin?

As one who has prescribed "Atophan" since it first appeared in Australia, I would give a negative reply to both questions. I consider that "Atophan" should be used only when the patient is under medical care and seen at regular intervals by the medical attendant. Personally I do not allow patients to take "Atophan" for more than two consecutive weeks and insist on seeing them several times during that period. I have also at times congratulated myself that I have been able to see the patient and discontinue the drug.

In elderly persons leading a sedentary life the action of "Atophan" on the liver may cause symptoms at short notice.

The public is already asking the chemist for "Atophan" tablets and is obtaining them. If, as in the case of aspirin, an "Atophan" appetite developes, I feel sure we shall find that it is time a warning was sounded.

Yours, etc.,

A. J. CORFE, M.B., Ch.M.

Glen Innes, New South Wales.
May 14, 1928.

CHRISTIAN SCIENCE.

SIR: In your issue of April 14, you add a footnote to my reply to a statement by Dr. Bostock, in which you say that the medical view of Christian Science is that "it is based on untenable hypotheses and conceived without the critical aspect which is so essential in scientific work."

Dr. Bostock in the issue of May 5 endorses this opinion and supplements it with further criticism of a destructive nature.

The medical world, prior to the advent of Christian Science, disregarded almost entirely the mental factor in the cause and cure of disease. It is now being recognized that it is the phenomenal success of the Christian Science practitioner, working along the lines of healing by spiritual processes alone, that has stimulated so much inquiry and research by the regular medical practitioner into the realm of psychoanalysis and other mental methods of healing.

Science, according to the Standard Dictionary, is the study of facts, principles and causes. Speaking on this phase of her work, Mrs. Eddy, in "Retrospection and Introspection," page 24, says: "During twenty years prior to my discovery I had been trying to trace all physical effects to a mental cause; and in the latter part of 1866 I gained the scientific certainty that all causation was MIND and every effect a mental phenomenon." On page 111 of the textbook, "Science and Health with Key to the Scriptures," she further states that after a lengthy examination of her discovery and its demonstration in healing the sick she submitted her metaphysical system of treating disease to the broadest practical tests and has proved itself, whenever scientifically employed, to be the most effective curative agent in medical practice.

The doctor truly remarks that "the true perspective can only be reached after impartial research into all accompanying circumstances." Mrs. Eddy's discovery was the outcome of the application of this rule, for her work embodied all the requirements of a scientific method—inquiry and proof, extending to the basing of the system on law.

If the doctor has had some patients who had not been healed by Christian Scientists, I can assure him that the great majority of the Christian Science Army, now numbering millions, are those whom the ordinary methods had failed even to relieve.

There is need for all those engaged in the healing art, no matter what the school, to be modest in their statements, for much yet remains to be done.

The criticism of the doctor and yourself against Christian Science is not justified on the facts, and could more fairly be levelled at medicine, for being largely an experimental science, its theories are changing every day and the hypothesis of today is discarded tomorrow.

Yours, etc.,

JOSEPH F. TURNER.

Christian Science Committee on Publication,
310, George Street,
Sydney.

[It is not a fact that "Christian Science" laid the foundation of treatment by psychological methods, but it is a fact that "Christian Science" methods are pure suggestion. The phenomenal successes of "Christian Science" have the same relation to reality as has the doctrine of Mrs. Eddy that there is no such thing as physical disease. The millions of Mrs. Eddy's blind followers have no more right to claim infallibility than have the hundreds of millions of non-Christians. Science means knowledge of facts. Mrs. Eddy and her followers have made a bad guess at facts.—EDITOR.]

THE BRANCHES OF THE BRITISH MEDICAL ASSOCIATION IN AUSTRALIA.

SIR: In your leader of May 12, 1928, "Looking into the Future," the following paragraph occurs:

> It was thought by the Queensland Branch that if an association were formed in Australia with a constitution similar to that of the Medical Association of South Africa (British Medical Association) the Branches might be independent of the governing influence of the Council of the British Medical Association and yet retain quite close bond with this great body.

This is not quite a correct description of the attitude of the Queensland Branch, because at no time did the Branch wish to be "independent of the governing influence of the Council of the British Medical Association." It was its desire that some arrangement might be made by which the affairs of the Australian Branches of the British Medical Association could be dealt with under the British Articles of Association more promptly than they sometimes are and their ardent wish was that some such arrangement should be made without disturbing the right of the home Association to govern.

Sitting as a delegate on the recent Federal Committee in Melbourne I endeavoured to make this quite clear. I feel sure that the members of the Branch would regret that the suggestion should be made that they had ever desired independence. After all, there can be no "close bond" without dependence.

Yours, etc.,

E. SANDFORD JACKSON.

THE LIGATURE AFTER SNAKE AND SPIDER BITE.

SIR: Since writing my last letter to the journal (May 5) on the use of the ligature after spider bite, I have been searching for any observation that would indicate the presence of thrombase in spider venom. I have found

the following, which appears to indicate that thrombase, or a similar body, is present in the poison of *lathrodectes*, the group that our red spot spider belongs to. It appears that Kobest in his researches on the Crimean karakurtes (*Lathrodectes erebus*) found that the venom of the karakurtes was a true toxin. Boiling rendered it completely inactive and alcohol had the same effect. It had a hæmolytic action and promoted coagulation. As these researches were carried out nearly thirty years ago, I doubt if thrombase had then been discovered. But the fact remains that the venom of the *lathrodectes* contains a body that coagulates the blood and so the ligature may be of use, for it may alter the nature of the venom and it may delay the absorption and this is important for the child that died in Sydney some months ago after being bitten by a red back spider, died within an hour.

Yours, etc.,

STEWART MCKAY.

Sydney.
May 14, 1928.

Books Received.

ACUTE APLASTIC ANÆMIA: ITS RELATION TO A LIVER HORMONE, by A. Hayes Smith, with pathological details of the case by C. J. Young; 1928. London: H. K. Lewis and Company, Limited. Royal 8vo., pp. 88. Price: 6s. net.

THE AMERICAN ILLUSTRATED MEDICAL DICTIONARY, by W. A. Newman Dorland, A.M., M.D., F.A.C.S.; Fourteenth Edition, Revised and Enlarged with the collaboration of E. C. L. Miller, M.D.; 1927. Philadelphia: W. B. Saunders Company; Melbourne: James Little. Royal 8vo., pp. 1388. Price: 37s. 6d. net.

NEOPLASTIC DISEASES: A TREATISE ON TUMORS, by James Ewing, A.M., M.D., Sc.D.; Third Edition, Revised and Enlarged; 1928. Philadelphia: W. B. Saunders Company; Melbourne: James Little. Royal 8vo., pp. 1127, with illustrations. Price: 63s. net.

COLLECTED PAPERS OF THE MAYO CLINIC AND THE MAYO FOUNDATION, Edited by Mrs. M. H. Mellish, H. Burton Logie, M.D., and Charlotte E. Eigenmann, B.A.; Volume XVIII; 1927. Philadelphia: W. B. Saunders Company; Melbourne: James Little. Royal 8vo., pp. 1353, with illustrations. Price: 60s. net.

BRAIN AND MIND OR THE NERVOUS SYSTEM OF MAN, by R. J. A. Berry, M.D., F.R.C.S., F.R.S. (Edinburgh); 1928. New York and Melbourne: The Macmillan Company. Royal 8vo., pp. 620, with illustrations. Price: $8.00 net.

Diary for the Month.

MAY 31.—New South Wales Branch, B.M.A.: Branch.
MAY 31.—South Australian Branch, B.M.A.: Branch.
MAY 31.—Northern Districts Medical Association, New South Wales.
MAY 31.—Illawarra Suburbs Medical Association, New South Wales.
JUNE 1.—Queensland Branch, B.M.A.: Branch.
JUNE 5.—Tasmanian Branch, B.M.A.: Council.
JUNE 6.—Victorian Branch, B.M.A.: Branch.
JUNE 6.—Western Australian Branch: Council.
JUNE 6.—South Sydney Medical Association, New South Wales.
JUNE 7.—South Australian Branch, B.M.A.: Council.
JUNE 8.—Queensland Branch, B.M.A.: Council.
JUNE 12.—Tasmanian Branch, B.M.A.: Branch.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xvi.

AUSTIN HOSPITAL FOR CHRONIC DISEASES, HEIDELBERG, VICTORIA: Honorary Pathologist.
CHILDREN'S HOSPITAL, CARLTON, VICTORIA: Medical Superintendent.
MELBOURNE HOSPITAL: Honorary Vacancies.
SYDNEY HOSPITAL: Honorary Gynæcological Surgeon, Honorary Assistant Gynæcological Surgeon.
THE ADELAIDE CHILDREN'S HOSPITAL, INCORPORATED: Honorary Vacancies.
THE WOMEN'S HOSPITAL, CROWN STREET, SYDNEY: Honorary Assistant Anæsthetist, Relieving Medical Officer.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham Dispensary. Manchester United Oddfellows' Medical Institute, Elizabeth Street, Sydney. Marrickville United Friendly Societies' Dispensary. North Sydney United Friendly Societies. People's Prudential Benefit Society. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Members accepting appointments as medical officers of country hospitals in Queensland are advised to submit a copy of their agreement to the Council before signing. Brisbane United Friendly Society Institute. Stannary Hills Hospital.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Contract Practice Appointments in South Australia. Booleroo Centre Medical Club.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Medical practitioners are requested not to apply for appointments to positions at the Hobart General Hospital, Tasmania, without first having communicated with the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales.

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